# GENETIC TESTING AND SCREENING IN THE AGE OF GENOMIC MEDICINE

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The New York State Task Force
On Life and the Law

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# Contents

# Preface

The New York State Task Force on Life and the Law was created by executive order in 1985 and charged with recommending policy on a host of issues raised by medical advances, including the determination of death, the withholding and withdrawal of life-sustaining treatment, organ transplantation, and assisted reproductive technologies. For each issue that the Task Force addresses, it recommends policy for New York State in the form of legislation, regulation, public education, or other measures. Seven of the Task Force's recommendations for legislation or regulation have been enacted in New York State.

This latest report is the result of a comprehensive study of clinical genetic testing and screening. The project leading to this report was undertaken at a time when startling new research and technological developments from the Human Genome Project, an international research project initiated in 1990, were just beginning to usher in a new age of genomic medicine. A national focus on the promises and risks of human genetics research for health care and the special programmatic attention by the U.S. Human Genome Project to the ethical, legal, and social implications of clinical genetic testing prompted the Task Force to examine these issues.

In the fall of 1993, the Task Force established a special committee on genetic testing and screening. The special committee worked with a group of experts in human genetics who served as consultants to the Task Force and identified issues in need of further consideration. The Task Force also held a two-day conference in which invited experts in diverse issues in genetic testing and screening introduced the full Task Force to the subject. In October 1994, the Task Force held an additional meeting on issues concerning genetic testing. In the fall of 1997, with generous funding from the National Human Genome Research Institute's Ethical, Legal, and Social Implications (ELSI) Program and the Greenwall Foundation, the Task Force turned its full attention to addressing the ethical, legal, and policy questions posed by advances in human genetics research, with a focus on the predictive uses of genetic testing. The Task Force's deliberations on these questions extended from the fall of 1997 to the summer of 2000.

The Task Force began this project by assessing the federal and state policy and legislative landscapes, with special attention to 1996 New York State legislation that addressed some concerns associated with clinical predictive genetic testing. In the first year of the project, the Task Force invited experts to its monthly meetings to make formal presentations on a wide range of issues. These issues included the current state of clinical genetics practice, the benefits and risks of state newborn screening programs, confidentiality of genetic testing information, informed consent for predictive genetic testing, oversight and quality assurance of clinical genetic testing laboratories, genetics research using samples obtained in the clinical context, and the benefits and risks of genetics research for members of different ethnic and racial groups.

The Task Force also performed research to assess the scientific and medical developments prompted by the Human Genome Project and the issues that these developments raise in the clinical care arena. As part of this research, the Task Force requested the input of practicing New York State clinical geneticists on several issues, such as New York State oversight of genetic testing laboratories and the role of genetic counselors, nurses, and primary care physicians in clinical genetics practice. The Task Force canvassed clinical genetic testing laboratories that are licensed by the New York State Department of Health and requested samples of their educational materials, official policy statements, and informed consent documents; the Task Force also solicited comments from these laboratories about the perceived value, strengths, and weaknesses of New York's laboratory oversight program. To assess third-party payer coverage of predictive genetic testing and genetic counseling services, the Task Force staff performed telephone interviews with the major health insurers in New York State. The Task Force convened meetings with groups of clinical and public health genetics professionals, including genetic counselors, and with representatives of the New York State Insurance Department. Task Force staff also attended national and local meetings of genetics professionals and advocacy groups.

The participation of clinical genetics professionals and other experts was critical to the deliberations of the Task Force. For their formal presentations to the group, we thank Ellen W. Clayton, M.D, J.D.; Jessica Davis, M.D.; Norman Fost, M.D.; Gail Geller, Sc.D.; Janlori Goldman, J.D.; James Hodge, Jr., J.D.; Neil Holtzman, M.D.; Eric Juengst, Ph.D.; Muin Khoury, M.D., Ph.D.; David Korn, M.D.; Robert Murray, Jr., M.D.; Thomas Murray, Ph.D.; Martin Natowicz, M.D., Ph.D.; Harry Ostrer, M.D.; Kenneth Pass, Ph.D.; Patricia Roche, J.D.; Karen Rothenberg, J.D.; Katherine Schneider, M.S.; Yvonne Thornton, M.D.; Ann Willey, Ph.D., J.D.; Lois Wingerson; and Randi Zinberg, M.S. For their participation in Task Force meetings or invited panels of clinical and public health genetics professionals, and/or for their review of draft portions of this report, we thank, in addition to some of those listed above, Alan Bombard, M.D.; Karen Brown, M.S.; Michele Caggana, Sc.D.; George Cunningham, M.D., M.P.H.; Luba Djurdjinovic, M.S.; Karen Greendale, M.S.; Katharine Harris, M.S.; Nanette Healy; Kurt Hirschhorn, M.D.; John Jacobi, J.D.; Elinor Langfelder, M.S.; Deborah Lochner Doyle, M.S.; Margaret McGovern, M.D., Ph.D; Susan Panney, M.D.; Elsa Reich, M.S.; Peter Rowley, M.D.; and Lawrence Sturman, Ph.D. We also extend our gratitude to others, too numerous to list, who generously offered guidance throughout the project.

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# Executive Summary

## Genes and Chromosomes

- Genes are the blueprints of heredity. Genes are made of hundreds to thousands of DNA bases.

- Each gene directs cells to produce one or more specific proteins, including enzymes and structural proteins.

- The human genome is the complete set of genes that every person inherits from his or her parents. It is present in virtually every cell of the body.

- The human genome consists of tens of thousands of pairs of genes. Each person inherits one copy of each gene from each parent.

- Genes are organized along string-like structures called chromosomes. Each individual inherits two sets of twenty-three chromosomes, one from each parent: two sets of twenty-two autosomes and one set of sex chromosomes (X, X or X, Y).

## Genetic Variations, Mutations, and Human Disease

- The DNA base sequence of human genes is about 99.9 percent identical among individuals. About 1 of every 1,000 DNA bases varies among individuals, accounting for inherited differences in traits and disease susceptibility.

- Changes in a DNA base sequence, called mutations, account for inherited gene variations. Mutations may be harmful if they prevent a gene from making a normal copy of its specific protein. These mutations can cause, or increase susceptibility to, specific diseases.

- Single-gene diseases are relatively rare diseases that result when a person inherits one gene with a harmful mutation or a pair of genes in which each has a harmful mutation. Inheritance of these mutated genes generally results in a 100 percent chance of developing a specific disease. Single-gene diseases include autosomal dominant diseases (e.g., Huntington disease), autosomal recessive diseases (e.g., sickle cell disease), and X-linked diseases (e.g., Duchenne muscular dystrophy).

- Most diseases result from a complex set of both genetic and environmental causes. Inheritance of some harmful gene mutations increases the chance, although it does not ensure, that a person will develop a specific disease. These mutations are called inherited susceptibility mutations.

## The Human Genome Project and Health Care

- The Human Genome Project, an international research project, has now deciphered the more than three billion DNA letters of the human genome. Follow-up research is expected to discover the structure and function of thousands of new genes.

- Genetics research will lead to the development of new predictive and diagnostic genetic tests. It also will lead to the development of new preventive and treatment interventions. Generally, the development of interventions lags years, even decades, behind gene discovery and genetic test development.

## Genetic Testing

- Genetic testing for inherited genetic variants is performed for several purposes: diagnosis of individuals with symptoms, determination of future disease risks in asymptomatic individuals, determination of genetic risks for progeny, guidance of medical treatment, research, and individual identification.

- Genetic testing for inherited genetic disease risks is an analysis of DNA, chromosomes, or gene products to provide specific information about variations in the number or form of genes or chromosomes in an individual or his or her progeny.

- Genetic information is information about specific variations in genes or chromosomes learned by genetic testing or by other means.

- DNA-based testing directly analyzes the DNA base sequence of a gene.

- Phenotypic testing identifies specific inherited gene variations indirectly, by detecting specific variations in the structure of a protein encoded by a gene or variations in a protein's enzyme activity.

- Karyotype analysis and fluorescent in situ hybridization analysis detect variation in form or number of chromosomes.

- New testing technologies that will promote genetic testing in health care include DNA chip technology and tandem mass spectrometry.

## Assessing the Accuracy and Usefulness of Genetic Tests

- Analytical validity of a genetic laboratory test is a measure of how well the test detects what it is designed to detect. It encompasses analytical sensitivity (the

probability that the test will detect a gene variant it is designed to detect when present in a sample) and analytical specificity (the probability that that the test will be negative when a specific variant tested for is not present in a sample).

- Clinical validity measures the extent to which an analytically valid test result can diagnose a disease or predict future disease. For predictive genetic tests, it includes positive predictive value (the ability to predict that an individual will develop a disease) and negative predictive value (the ability to predict that an individual will not develop a disease).

- For DNA-based testing, clinical validity is limited by genetic heterogeneity and incomplete penetrance. Genetic heterogeneity means that different mutations in a specific gene, or mutations in different genes, are associated with the same disease. Incomplete penetrance means that within a population, not everyone who tests positive for a specific gene mutation will develop the associated disorder.

- Utility of a test is a measure of how useful test results are to the person tested. Clinical utility is a measure of how a test may guide clinical decisions. In some circumstances, predictive genetic testing may not provide medical preventive or treatment options but may help reduce anxiety and/or aid planning for the future.

## Predictive Genetic Testing to Assess Reproductive Risks

- Reproductive genetic tests detect heritable genetic variations that are associated with disease. This type of testing includes carrier testing, prenatal testing of fetal cells, and pre-implantation testing of embryos formed by in vitro fertilization.

- Reproductive genetic tests generally are offered to individuals and couples who are at increased genetic risk for a specific disorder based on family history or membership in a racial or ethnic group that has identified genetic variants that increase risk for a specific disease.

- Carrier testing generally is performed to determine the risk of a healthy individual or couple of having a child with a recessive disorder. It may be performed before or after conception.

- Prenatal testing of fetal cells includes amniocentesis and chorionic villus sampling.

- Pre-implantation testing of embryos formed by in vitro fertilization is performed using single cells removed from individual embryos to detect specific gene mutations or chromosomal anomalies.

## Predictive Genetic Testing to Assess Future Disease Risks in Healthy Adults

- Presymptomatic genetic testing is predictive testing of apparently healthy adults to determine whether they are at risk for a single-gene disorder. These disorders occur with virtually 100 percent incidence in persons who have inherited a specific gene mutation.
- Susceptibility (predispositional) testing is predictive genetic testing of apparently healthy adults to determine whether they are at increased risk, relative to the general population, for a specific future disease. A positive test result (finding a mutation) does not necessarily mean that a person will develop a future disease.

- For susceptibility testing, establishing a test's clinical predictive value may require years of research.

- Pharmacogenetic testing is genetic testing of individuals to guide their pharmaceutical or other medical treatment. Pharmacogenetic testing seeks to promote a favorable response and to prevent an adverse response to a drug or other treatment based on genetic predisposition.

## Misunderstandings of and Misperceptions about Genetics

- Throughout human history, people have understood that physical and behavioral traits have a genetic component. Proponents of a centuries-long debate, referred to as the "nature-nurture" debate, have disagreed about the relative contribution of genetic and environmental factors to human behavioral and cognitive (intelligence) traits.

- Scientific evidence, including evidence from molecular genetics research, shows that genes may influence complex behavioral and cognitive traits and mental illness. Generally, however, behavioral and cognitive traits and mental illnesses result from a complex and cumulative interplay of many genetic and environmental factors.

- Many commentators express concern that the general public and the popular press overemphasize the role of genetic inheritance for health as well as for the development of behavioral and cognitive characteristics, taking an overly deterministic view of genetics. These views may lead people to overestimate the meaning of genetic testing and to misconstrue genetic test results.

- Throughout the past century, some countries, including the United States, have promoted and/or endorsed eugenic policies that aim to promote the births of certain types of individuals and to discourage births of other types of individuals.

- In the first half of the twentieth century, eugenic attitudes contributed to the passage of federal legislation to limit immigration of people into the United States based on country of origin. Eugenic attitudes also were a cause of federal and state court decisions and state legislation that prevented or discouraged marriages of people from different racial groups and promoted involuntary sterilization of individuals who were deemed "unfit." Included among the "unfit" were the mentally ill, the "feebleminded," and habitual criminals.

- "Genetic exceptionalism" is the belief that medical genetics is sufficiently different from other areas of medicine to warrant special protections. Commentators disagree on whether genetic testing should be treated differently from other forms of medical testing.

- Genetic testing shares characteristics with other forms of medical testing. However, some forms of predictive genetic testing, notably DNA-based testing of inherited genetic variants, differ from other medical testing in important ways. For example, predictive DNA-based genetic testing has exceptionally long-range predictive powers; it can predict disease, or increased risk for disease, in the absence of clinical signs or symptoms; it reveals the sharing of genetic variants within families at precise and calculable rates; and, at least theoretically, it has the potential to generate a unique identifier profile for individuals.

## Genetic Screening for Adult Health and Reproductive Risks

- Genetic screening differs from genetic testing in that it targets populations rather than at-risk individuals. Genetic screening generally is performed to detect future disease risks in individuals or their progeny for which established preventive interventions exist. Examples of genetic screening include newborn screening for phenylketonuria, carrier screening for sickle cell disease, and prenatal screening of fetal cells to detect chromosomal or other congenital abnormalities.

- Although predictive genetic screening to detect future disease risks in adults has not yet been offered, commentators predict that predictive genetic screening for hemochromatosis and other adult-onset diseases will be offered in the next decade.

- Some commentators express concern that if screening tests become routine practice, individuals may be pressured to undergo testing that they would not choose to undergo in a different context. Commentators also express concern about possible discrimination and/or stigmatization against individuals and groups who are the subjects of genetic screening because of their racial, ethnic, or geographic origin.

- Commentators maintain that a number of factors should be evaluated in determining whether a particular screening test should be implemented, including the purpose of the screening test, the test's analytical validity, clinical validity, and clinical utility, and the cost of the screening test.

- Multiplex genetic testing is genetic testing for two or more completely different conditions in a single testing session. Some commentators oppose multiplex genetic testing if it is performed only because it is technologically possible. Other commentators maintain that multiplex genetic testing is generally inappropriate unless the tests provide clear and useful options to the persons being tested. A key issue for both reproductive and late-onset multiplex testing is how to bundle tests together to allow for appropriate pretest education, counseling, and consent.

**Conclusions and Recommendations of the Task Force**

***Purpose of Predictive Genetic Screening***

- The purpose of predictive genetic screening should be to benefit the individual or couple tested. Screening tests offered to healthy individuals who do not perceive themselves or their offspring to be at increased risk for disease based on family and/or personal history should provide clear medical benefits or expanded reproductive options.

***Predictive Value of Screening Tests***

- Predictive genetic screening tests should have a sufficient level of confirmed predictive value in healthy populations to justify their use for individuals who are not known to be at increased disease risk.

***How to Offer Predictive Genetic Screening Tests***

- Predictive genetic screening tests should be voluntary and should be offered only when accompanied by adequate education, counseling, informed consent, test follow-up, and efforts to ensure confidentiality.

***Special Concerns about Offering Genetic Screening to Determine Risks for Late-Onset Disorders***

- Genetic screening tests to determine future risk for late-onset disorders should have confirmed clinical utility, and screening should be offered on an age-appropriate basis to ensure maximum medical benefit and minimal risks.

***Special Concerns about Offering Genetic Screening to Determine Reproductive Risks***

- Genetic screening tests to predict reproductive risks should provide individuals and couples with useful options. Providers should make clear that despite the routine offering of tests, some individuals may wish to decline if they think that the test will not be useful to them. Providers should offer screening tests in a timely manner to maximize the reproductive options of tested individuals.

***Federal and State Governments Should Not Require Genetic Screening by Law***

- It is generally inappropriate for federal or state governments to mandate population genetic screening. New York State should repeal legislation that mandates sickle cell carrier screening for some couples seeking a marriage license.

***Role of Study Panels and Professional Guidelines***

- Study panels that include national experts, community representatives, and others, as well as professional medical societies such as the American College of Obstetricians and Gynecologists and the American College of Medical Genetics, should determine the appropriateness of offering specific genetic screening tests based on the test's validity and utility. For reproductive screening tests, for which follow-up options may include decisions about pregnancy termination, professional guidelines should consider the seriousness of the disorder tested for, its penetrance, its age of onset, and the variability of disease symptoms.

***Genetic Screening of Minors***

- Generally, minors should not be offered genetic screening tests to determine future health or reproductive risks, unless screening provides a clear and timely medical benefit and has minimal psychosocial risks.

***Multiplex Genetic Testing Panels***

- Genetic tests that provide information about future risks for unrelated disorders should be included in multiplex testing panels only when they meet all criteria for genetic screening tests. Tests should be grouped based on similar issues and implications to allow for adequate counseling and consent. For tests to determine risks for late-onset diseases, tests placed in multiplex panels should provide a demonstrated, significant medical benefit and should be offered on an age-appropriate basis. For reproductive carrier testing, tests placed on a multiplex panel should be for diseases of similar seriousness.

## Newborn Screening

- Newborn screening is the most widely performed type of genetic testing in the United States today. Newborn screening programs exist in all fifty states, the District of Columbia, Puerto Rico, and the Virgin Islands. The goal of newborn screening is to detect infants affected by

conditions for which prompt application of confirmed interventions can prevent or reduce disease, disability, and/or death.

- As a result of the Human Genome Project, the discovery of the genetic variations that underlie inherited disorders and the technology to detect them are expanding rapidly. These developments will present state screening programs with new testing methods and expanded lists of disorders for which testing is possible.

- Most states, including New York, have added tests to their newborn screening panels without formal criteria or processes to guide them. Many commentators recommend that newborn screening programs form advisory committees composed of medical and laboratory professionals and community participants to establish criteria for screening tests and to review screening test panels and program outcomes.

- Most states, including New York, mandate newborn screening and do not require parental consent. New York and other states exempt from newborn screening children whose parents have religious objections to it. Commentators disagree over whether parental consent to newborn screening should be required.

- Some benefits of newborn screening are reduced morbidity and mortality of children and cost savings to society through early prevention and treatment of childhood disease. Some of the risks of newborn screening include parental anxiety about false positive results; harm that can be caused to the parent-child relationship by parental misperceptions about the meaning of a child's carrier status; and the possibility that children will be subjected to needless, and potentially risky, medical interventions or monitoring.

- Most newborn screening programs, including New York's program, store residual newborn blood samples (bloodspots) and use them for research. Some commentators maintain that it is appropriate to use residual screening samples for research if the samples are anonymized. Others contend that ethical concerns about the use of residual newborn blood samples may be greater than for other tissue samples obtained in the clinical context because the collection of newborn screening samples is mandated by law. Commentators also have discussed the appropriate research uses of identified and coded newborn samples and whether parental consent for and/or notification about the research use of residual newborn screening samples should be required.

**Conclusions and Recommendations of the Task Force**

***Basic Requirements for Newborn Screening Tests***

- New York's Newborn Screening Program panel should be restricted to tests that detect congenital disorders characterized by serious and irreparable harm that can be avoided or minimized only by prompt application of confirmed medical interventions. The analytical and clinical validity of the screening tests also must be confirmed.

***Statutory Authorization for New York's Newborn Screening Program***

- New York Public Health Law § 2500-a should be amended to delete the names of individual disorders screened for by the Newborn Screening Program. The law should designate the Commissioner of Health to specify in regulations those congenital disorders for which screening should be performed.

***Informing Parents about Newborn Screening***

- The Commissioner of Health should promulgate regulations to require the Newborn Screening Program to provide educational materials about screening to prenatal care providers, as well as to hospitals and institutions of birth. Prenatal care providers should be required to provide and be available to discuss these materials during the course of prenatal visits. Program materials should be multilingual and at appropriate reading levels for a general audience. They should explain the purpose of screening and provide a description of the disorders screened for, their population incidence, and the follow-up process for infants with a positive screen test result.

***Mandatory Newborn Screening***

- New York's Newborn Screening Program should be mandatory for all infants born within the state, provided that several conditions are met: (1) all screening tests must meet the criteria described above in the recommendation concerning the basic requirements for newborn screening tests; (2) parents must be informed and receive educational materials about the program, its goals, and the screening process; and (3) the state must ensure that newborns identified as positive in screening tests are promptly diagnosed and that identified newborns and their families have access to follow-up medical care and counseling related to the disorder, regardless of their ability to pay. New York Public Health Law § 2500-a should be amended to remove the right of parents to assert religious objections to screening.

***Follow-up Evaluation and Diagnosis of Screen-Positive Newborns***

- The Newborn Screening Program should ensure that follow-up testing and diagnostic evaluation of newborns who test positive on a screening test is rapid and readily accessible, to maximize treatment benefits for affected newborns and to minimize potential anxiety associated with an initial false positive test result.

***Follow-up Medical Care for Newborns of Confirmed Positive Newborns***

- New York State should ensure that newborns detected to have a congenital condition by newborn screening receive necessary long-term medical and preventive care, into and through adulthood, regardless of ability to pay. The Newborn Screening Program should facilitate efforts to ensure that affected newborns identified by the program obtain necessary and appropriate medical care. The program should assist treatment centers in locating and treating children who are lost to follow-up.

***Establishment of a Newborn Screening Advisory Committee***

- New York's public health regulations should establish a newborn screening advisory committee to act in an advisory capacity to the Commissioner of Health and the Newborn Screening Program. The committee should include outside professional and community representatives and should be independent from the screening program. It should meet at least annually to consider new screening tests, solicit community input, and evaluate program infrastructure, policies, and outcomes.

***Review and Implementation of Newborn Screening Tests***

- A newborn screening advisory committee, and ad hoc specialty subcommittees established by it, should review all tests currently on or under review for New York's screening panel, as well as potentially valuable new tests, and make recommendations to the Commissioner. For tests for which a confirmed medical benefit has not been sufficiently demonstrated, tests should be viewed as human subject research and should require parental informed consent. These tests should be subject to review by an institutional review board to determine the information that should be provided as part of obtaining parental informed consent. All new screening tests should be subject to periodic follow-up evaluation to determine test accuracy and effectiveness of medical interventions.

***Universal Performance of Newborn Screening***

- Newborn screening tests should be performed for all newborns, rather than targeted to specific minority populations perceived to be at higher-than-average risk for a particular disorder.

***Financing of the Newborn Screening Program***

- A permanent, stable funding source is needed to enable the program to consider additional tests, implement new tests as needed, consider changes in testing

technologies, improve processes and follow-up evaluation, and support the activities of the advisory committee.

***Research Use of Anonymized Newborn Bloodspots***

- The Newborn Screening Program, consistent with the recommendations in Chapter 7 concerning research use of samples obtained in the clinical context, should permit the use of anonymized samples for research. The program should inform parents that residual bloodspots may be anonymized and used for quality assurance activities or research. Parents should be informed of the potential research value of the samples and of the impossibility of linking research results to any individual newborn.

***Research Use of Identified Newborn Bloodspots***

- Research use of identified newborn bloodspots should be permitted in accord with recommendations in Chapter 7 concerning the research use of identified samples obtained in the clinical context. In addition, investigators who seek to use identified newborn blood samples for research should demonstrate why unidentified samples or alternate sample sources would not suffice. The use of identified samples should require recontact by the New York State Department of Health and informed consent of parents for each research use. The New York State Department of Health should not release samples that retain identifying data to researchers outside the department except for rare circumstances in which the research is directly relevant to the health of a specific newborn.

***Research Use of Coded Newborn Bloodspots***

- Research use of coded newborn bloodspots should be permitted in accord with recommendations in Chapter 7 concerning the research use of coded samples obtained in the clinical context. The use of coded samples should require recontact by the New York State Department of Health to obtain the consent of parents for the future research use of the samples.

***Policies for Storage of Newborn Bloodspots***

- The Newborn Screening Program should establish a formal policy for the storage of residual identified and anonymized bloodspots. The policy should specify potential uses for stored bloodspots and a maximum period of time for which samples may be maintained with personal identifiers.

***Notification of Parents of Newborn Carrier Status***

- When carrier status for a recessive genetic disease is determined as an incidental finding of a newborn screening test, New York's Newborn Screening Program should report that finding to the authorized physician. Ideally, parents of carrier newborns should be

informed of that result and offered appropriate education, counseling, and testing by appropriately trained and credentialed professionals.

## Informed Consent

- Informed consent to a medical procedure is an agreement to allow a medical procedure to go forward after having been advised of relevant facts necessary to make that agreement an intelligent one. Relevant facts include the patient's diagnosis, the nature and purpose of the proposed procedure, and the risks and benefits of, and the alternatives to, the procedure.

- Obtaining a patient's informed consent to medical procedures is both a legal necessity and a basic requirement of medical ethics, and most commentators maintain that the requirement of informed consent applies to decisions about predictive genetic testing. Some of the issues that commentators recommend that health care providers should discuss with their patients as part of obtaining informed consent to predictive genetic testing include: (1) the purpose of the test; (2) a description of the testing process; (3) the accuracy of the genetic test and the meaning of its results; (4) the risks and benefits of, and alternatives to, genetic testing; and (5) confidentiality issues.

- It is unclear whether New York's general law on informed consent to medical procedures covers predictive genetic testing. However, in 1996 and 1997, New York enacted laws that require persons performing predictive genetic tests to obtain the individual's written informed consent prior to testing. The laws require the consent form to contain some, but not all, of the information commentators have recommended for informed consent to predictive genetic testing.

- Multiplex genetic testing is predictive genetic testing for more than one condition in a single testing session. Some commentators argue that health care providers should obtain full informed consent from patients for each test in a multiplex testing panel. Others contend that a patient's generic consent to all of the tests in the panel would be sufficient if the consent process highlights broad concepts and common-denominator issues for all of the tests.

- Commentators disagree about the proper method for obtaining informed consent to predictive genetic tests for gene variants that have been identified as having multiple, seemingly unrelated health effects (pleiotropic genetic tests). One contends that health care providers have an obligation to disclose to patients the risks associated with learning information about all of the conditions detected by the tests and must provide counseling and other support services as required by testing protocols for each individual condition. Another maintains that outside of the reproductive genetic testing context and situations where there are "special concerns" about the

psychological state of a patient to be tested, health care providers need only inform their patients about the different clinical uses of the test and need not provide any special counseling or support services.

- Stored tissue samples, which today number at about 282 million in the United States, are used by medical researchers as their principal source of human biological materials. These tissues are most commonly collected during clinical medical procedures, and many of the patients from whom they are collected are not informed that their tissues will be stored and used for research.

- In some circumstances, federal regulations governing research involving human subjects require researchers to obtain a subject's informed consent before performing research on the subject's identified or coded tissue samples removed in the clinical context. These regulations do not require informed consent if the tissue samples have been anonymized. New York's statutes concerning research involving human subjects specifically exempt tissues removed in the clinical context from the statutes' coverage.

- Although most commentators agree that researchers should obtain a subject's informed consent before performing research on the subject's identified tissue sample, commentators disagree about whether, or what type of, consent is necessary before researchers may perform research on a subject's coded or anonymized tissue samples.

**Conclusions and Recommendations of the Task Force**

***Necessity of Informed Consent for Predictive Genetic Testing in the Clinical Context***

- Predictive genetic testing should not be performed without the informed consent of the subject of the test, except in the limited circumstances described below.

***Power of the Commissioner of Health***

- Those sections of New York's genetic testing statutes that list specific elements of informed consent should be replaced with an authorization for the Commissioner of Health to issue regulations on the process and content of informed consent to predictive genetic testing.

***Content of Informed Consent to Predictive Genetic Testing in the Clinical Context***

- Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require the following information to be provided to the patient before obtaining the patient's consent (elements currently not required by New York law are italicized):

1. The purpose of the test

2. A general description of the testing process

3. A description of the diseases or conditions tested for, *including their ranges of severity*

4. *The risks and benefits of, and alternatives to, the predictive genetic test*

5. Confidentiality issues, *including confidentiality protections, the circumstances under which results of tests may be disclosed without the patient's consent*, and the names of persons and/or organizations to whom the patient has consented to disclose the results

6. *Protections against adverse uses of genetic information*

7. *The chances of false positive and false negative results*

8. The meaning of both positive *and negative* results

9. *The ability, or lack thereof, of the test to predict a disease's severity and age of onset*

10. *The possibility that no additional risk information will be obtained at the completion of the test*

11. *Available medical surveillance, treatment, and/or reproductive options following testing*

12. A statement that, prior to providing informed consent to genetic testing and after receiving the results, the individual may wish to obtain professional genetic counseling

13. *The risks of transmitting the relevant mutation to children and that the mutation may be present in other blood relatives*

14. A statement that no tests other than those authorized will be performed on the biological sample and that the sample will be destroyed at the end of the testing process, or not more than a specific period of time after the sample was taken, unless the subject consents to a longer period of storage

15. *That the test is voluntary*

16. *An offer to answer inquiries*

17. *The fees charged for the laboratory tests and pre- and posttest counseling*

***Sufficiency of Signed Informed Consent Form as Evidence of Informed Consent***

- Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require that health care providers disclose the information described above in a manner that will enable the patient to make a knowledgeable evaluation. A signed informed consent form is not necessarily sufficient evidence that this goal has been achieved.

***Use of Decision Aids in the Informed Consent Process***

- Health care providers are encouraged to use decision aids, such as written materials, videos, group discussions, and CD-ROMs, as part of the informed consent process to predictive genetic testing. However, health care providers should not use decision aids as a substitute for discussing predictive genetic testing issues with their patients.

***Persons Required to Obtain Informed Consent***

- Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require that the person who orders a predictive genetic test has the obligation to ensure that the subject's informed consent is obtained.

***Responsibility of Testing Laboratories***

- The New York State Department of Health should permit clinical laboratories to perform predictive genetic tests on biological samples only if the laboratories receive assurances that the subjects provided informed consent for the tests.

***Professional Guidelines on the Process and Content of Informed Consent for Predictive Genetic Tests***

- Professional organizations should issue guidelines on the process and content of informed consent for specific predictive genetic tests and should create model consent forms that are consistent with existing law and contain the information necessary for patients to make informed decisions about undergoing predictive genetic testing.

***Health Care Providers Qualified to Order Predictive Genetic Tests***

- Health care providers should order predictive genetic tests only when (1) they know the circumstances under which it is appropriate to order them and the meaning of their results, (2) they are capable of providing their patients with sufficient information to make informed decisions about undergoing the tests, and (3) they are able to provide their patients with comprehensive pre- and posttest counseling or can refer their patients to professionals who are able to do so.

***Informed Consent to Multiplex Genetic Testing***

- Ideally, a patient's full informed consent should be obtained to each test on a multiplex panel prior to testing. However, assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, generic consent to multiplex testing should be permitted if (1) the number of tests on the panel is so high or the information about the tests is so complicated that attempting to obtain full informed consent from the patient to each test would be confusing or otherwise burdensome to the patient; (2) the tests on the panel meet all of the criteria described in Chapter 5 for inclusion in a multiplex panel; (3) the patients are informed, prior to testing, that more detailed information about each test is available; and (4) the patients are given an opportunity to obtain that information prior to testing either from the health care provider offering the multiplex panel or from another health care professional.

***Special Issues Related to Pleiotropic Information***

- Before offering a predictive genetic test to a patient, providers should give the patient all information necessary for the patient to provide informed consent to the intended use of the test, that is, information relevant to any condition about which the patient intends to receive test results. If the test also may reveal confirmed, clinically valid information about conditions for which the patient has not sought testing, the provider should inform the patient of this fact, specifying (1) the condition(s) about which the test may reveal information; (2) the consequences of having this additional information in his or her medical record; and (3) opportunities, including genetic counseling, for the patient to obtain further information about aspects of the test unrelated to its intended use. If the patient expresses an interest in learning how his or her test results relate to conditions for which testing was not originally sought, the provider should ensure that the patient provides informed consent to obtaining this additional information. Providers should respect patients' right not to learn pleiotropic information revealed by genetic tests.

***Court Orders for Predictive Genetic Testing***

- New York law should be amended to permit courts to order predictive genetic testing without the subject's consent only when (1) absent the testing, there would be a clear and imminent danger to the public health; (2) such testing is authorized by federal and/or New York State statutes or regulations; or (3) in a civil or criminal litigation, the subject affirmatively places his or her physical or mental condition at issue and the genetic testing directly relates to that physical or mental condition.

***Remedies for the Performance of Genetic Testing without Informed Consent***

- New York law should be amended to expressly authorize private lawsuits by subjects of unconsented-to predictive genetic tests against persons who order and/or perform the tests.

- New York law should be amended to authorize the Attorney General to bring lawsuits on behalf of individuals who have undergone predictive genetic testing without informed consent.

- Persons and organizations licensed by New York State should be subject to professional discipline and/or other sanctions, including fines and license suspension and revocation, for performing or ordering predictive genetic testing without informed consent.

***Research on Tissue Samples Obtained in the Clinical Setting***

- New York's law on the protection of human research subjects should be amended to cover research on tissue samples obtained in the clinical context. The amendment should apply only to tissue obtained after the amendment's effective date.

- Research on identified tissue samples obtained in the clinical context should be permitted only after the subjects have provided full informed consent to the research and an institutional review board has reviewed and approved the research protocol.

- Research on anonymized tissue samples obtained in the clinical context should be permitted only after an institutional review board has reviewed and approved the research protocol. The institutional review board review should ensure that the samples are or will be truly anonymized and should determine whether the research is of such a sensitive nature that it is inappropriate to use anonymized samples without having obtained the subjects' specific consent to the research.

- Research on coded tissue samples obtained in the clinical context should be permitted only if (1) the patients have agreed to the storage and research use of their coded samples; (2) the patients have been told about the operation, tissue release policies, and confidentiality protections of the tissue repository; and (3) an institutional review board has reviewed and approved the protocols for the research. The institutional review board review should ensure that the samples are or will be truly coded and should determine

whether the research is of such a sensitive nature that it is inappropriate to use coded samples without having obtained the subjects' specific consent to the research. The coding of the samples should be performed by a person who is not connected to the research and who will not learn the individual results of the testing.

- Patients should be informed that their decision about whether to consent to the research use of their coded and/or identified tissue samples is wholly voluntary and that their decision will not affect their access to, or quality of, care.

- Institutions should encourage clinicians to ask patients to consider authorizing the use of their tissue for research purposes, and clinicians should do so when they deem it appropriate.

## Predictive Genetic Testing of Children

- When susceptibility to a genetic disorder is discovered within a family, parents may seek predictive genetic testing of their children to obtain a medical benefit for the child, to reduce the child's future disease risk, and/or to make life planning decisions. Adolescents also may initiate requests for predictive genetic testing to determine future disease or reproductive risks.

- Parents generally have the legal authority to control their children's medical care, and children may generally not obtain medical care without their parents' consent.

- Benefits of testing children for late-onset disorders can include parental recognition of the need for clinical surveillance and/or preventive measures available for their asymptomatic children and enhanced parental ability to make life planning decisions for their children. Possible risks include the use of unconfirmed clinical interventions on the children that may be unnecessary and/or harmful, discrimination against the children, and psychological harms to the children and family.

- There are generally no benefits to genetic carrier testing of minors, except when adolescents are contemplating marriage or having children in the near future. Risks of such testing include stigmatization, discrimination, and parental misunderstanding of the meaning of the test results.

- Most commentators contend that the primary determinant of whether a child should undergo genetic testing is the best interests of the child. In the absence of a clear medical benefit to the child, these commentators opine that avoidance of potential testing-associated harms and the preservation of the minor's future autonomy should be the overriding considerations. Accordingly, these commentators maintain that

children generally should not undergo genetic testing for late-onset disorders in the absence of a medical benefit and should not undergo genetic carrier testing for recessive disorders.

- Most commentators agree that health care providers play an important role in assessing the benefits and risks of testing a child to the child and family.

**Adoption**

- New York mandates that adoption agencies disclose to prospective adoptive parents the "available" medical histories of the prospective adoptee and the child's biological parents. These histories must include all available information about diseases or conditions believed to be hereditary. New York law does not require parties to an adoption to exercise reasonable efforts to collect this information if it is not already available.

- Commentators stress that the best interests of the prospective adoptees should be the guiding principle in determining whether they should undergo genetic testing. Some commentators contend that prospective adoptees should undergo genetic testing only in situations where it would be appropriate to test other children.

**Conclusions and Recommendations of the Task Force**

***Predictive Genetic Testing to Determine Adult-Onset Disease and Reproductive Risks***

- The best interests of the child, including respect for the child's future autonomy, should be the primary consideration in decisions about predictive genetic testing of children. Predictive genetic testing of children is clearly appropriate when test results will provide information relevant to current decisions about the child's care, such as decisions to institute prophylactic treatment. Where the benefits to the child are less clear, however, predictive genetic testing should be approached with caution, given that testing can also lead to significant harms.

***Predictive Genetic Testing to Determine Risks for Pediatric-Onset Disease***

- When a healthy child is at risk for a pediatric-onset disorder, predictive genetic testing to confirm or allay disease risks may be in the best interests of the child, even if preventive or therapeutic interventions are not available.

***The Role of Health Care Providers in Guiding Predictive Genetic Testing Decisions***

- Health care providers play a critical role in guiding decisions about predictive genetic testing of children. When faced with a parent's request for predictive genetic testing of a healthy child or with a request initiated by a healthy adolescent, providers should

counsel the parents and the child, commensurate with the child's maturity, and help families balance potential benefits and risks of testing. When the balance of potential risks and benefits is uncertain, providers should generally respect the decisions of parents.

***Conflicts between Parents and Adolescents***

- Ideally, predictive genetic testing of children will be performed with both the consent of the parents and either the assent or consent of the child, depending on the child's maturity. The Task Force members hold differing views about cases where parents and adolescents disagree about genetic testing decisions. Where the balance of benefits and risks is uncertain, some members believe that providers should generally defer to the wishes of the parent, even over the objection of a mature adolescent. Others would defer to the adolescent's decision in at least some cases, particularly when an adolescent opposes testing.

***Disclosure of Test Results to Minors***

- If a child or adolescent has provided assent or consent for predictive genetic testing, he or she also should be informed of test results and their meaning, commensurate with his or her maturity and with his or her desire to have this information.

***Genetic Testing of Prospective Adoptees by Their Current Caregivers***

- Caregivers of prospective adoptive children should ensure that the children undergo genetic testing when such testing is necessary for the children's current health care.

***Genetic Testing of Prospective Adoptees at the Request of Prospective Adoptive Parents***

- Genetic testing should be performed on a prospective adoptee at the request of prospective adoptive parents only when (1) the testing is medically indicated and can reveal that a child is highly likely to develop extraordinary health care needs during childhood, (2) the testing will help ensure that the child is placed with a family who is capable of dealing with those needs, and (3) the prospective parents are otherwise committed to adopting the child.

***Collection and Disclosure of Prospective Adoptees' Medical Histories***

- New York law should be amended to require that parties placing a child for adoption make reasonable efforts to collect a complete medical and genetic history of the child and provide it to the prospective adoptive parents. New York law also should be

amended to require the parties to make reasonable efforts to collect the medical and genetic histories of the birth parents and close blood relatives of the prospective adoptee and disclose them to the prospective adoptive parents. The parties should collect and disclose this information in a manner that respects the privacy of the persons from whom it is obtained and the subjects of the information. For example, the medical and genetic histories of the prospective adoptees' relatives should be disclosed to prospective adoptive parents with all identifying information removed.

## Confidentiality

- Numerous persons and organizations, including insurance companies and the government, have access to individuals' health and genetic information.

- Although legal protections for health and genetic information confidentiality exist on both the federal and state levels, they are often limited in scope and do not provide adequate safeguards.

- Some commentators maintain that genetic information is more sensitive than other health information and should receive special confidentiality protections because it has been used in the past to discriminate and perpetrate terrible horrors against those deemed to be genetically unfit and because it reveals not only personal health information but also information that has implications for one's family. Other commentators contend that genetic information and nongenetic health information should receive the same levels of confidentiality protections because nongenetic health information can be just as sensitive as genetic information and it is impractical to provide varying levels of protection to different categories of health information.

- New York passed laws in 1996 and 1997 that provide greater confidentiality protections for predictive genetic information than for other health information. However, the laws do not protect the confidentiality of all genetic information, and they do not protect as confidential the fact that an individual has used or inquired about genetic services. The laws also do not provide individuals with legal remedies against those who violate the laws' provisions, do not appear to prohibit waiver of its confidentiality protections, and do not make clear whether anonymous genetic testing is permissible.

- Commentators disagree about whether health care providers ever have the obligation to disclose to a patient's relatives, over the patient's objection, the medical ramifications to the relatives of the patient's genetic information. Some commentators maintain that health care providers should not make such disclosures over the patient's objection and that health care providers should fulfill any obligations they might have vis-à-vis the patient's family by informing the patient of these ramifications and, when appropriate, advising the patient to disclose the information to the patient's family. Other commentators contend that health care providers should disclose the information directly to the patient's family, over the patient's objection, if the patient refuses to do so and if doing so would avert serious harm that is highly likely to occur absent such a disclosure.

- Some commentators have recommended that, to encourage individuals to take genetic tests and to prevent unconsented-to acquisition of genetic information by insurers, employers, and others, patients should be permitted to take certain types of genetic tests anonymously. Others believe that anonymous genetic testing is generally inappropriate because it interferes with proper pretest and posttest genetic counseling.

**Conclusions and Recommendations of the Task Force**

***Confidentiality Protections for Genetic Information and Other Medical Information***

- All personal medical information, including genetic information, should receive a uniform, high level of confidentiality protection. Absent new, comprehensive federal legislation or regulation that provides such protection, New York should enact comprehensive medical confidentiality legislation that does so.

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to protect the confidentiality of all genetic information.

***Confidentiality Protections for the Use of Genetic Services***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to protect the confidentiality of the fact that an individual has obtained and/or inquired about genetic testing and/or counseling. The statutes also should be amended to protect the confidentiality of the content of the inquiries and/or counseling.

***Scope of Consented-to Disclosure of Genetic Information by Persons Other Than the Subject of the Information***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to limit the disclosure of genetic information by persons other than the subject of the information to the amount necessary in light of the reason for the disclosure. The statutes also should be amended to limit such disclosures to those persons who have a need for the information in light of the reason for the disclosures.

***Permissible Third-Party Disclosures of Genetic Information without the Subject's Consent***

- Assuming that comprehensive medical confidentiality protections are not adopted, the legislature should review and, if appropriate, amend the genetic confidentiality statutes in light of the recommendations of the Special Committee on Medical Information Confidentiality of the New York State Public Health Council about legitimate disclosures of medical information without patient consent.

***Waivers of Genetic Confidentiality Protections***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to render nonwaivable all of the confidentiality rights they provide.

***Disclosure of Genetic Information to Relatives***

- Health care providers should discuss with their patients the medical ramifications of the patient's genetic information for the patient's relatives. Health care providers should encourage their patients to disclose genetic information to relatives when the disclosure is likely to help the relatives avert or treat disease or to make reproductive decisions. Health care providers should not disclose their patient's genetic information to the patient's relatives without the patient's consent or a court order. Courts should be authorized to permit health care providers to make such disclosures only when (1) the patient refuses to disclose the information to an identified relative despite attempts by the health care provider to convince him or her to do so; (2) without disclosure, serious harm to the relative is highly likely to occur; (3) with disclosure, the harm can be averted or its chances of occurring significantly minimized; and (4) the harm that may result from failure to disclose outweighs the harm that may result from the disclosure.

***Court Orders for Disclosure of Genetic Information***

- Other than court orders for the disclosure of genetic information to a patient's relatives, New York law should be amended to permit court orders for the disclosure of genetic information to third parties without the subject's consent only when (1) absent the disclosure, there is or would be a clear and imminent danger to the public health; (2) the third party is entitled to the disclosure under federal and/or New York statutes or regulations; or (3) in a civil or criminal litigation, the subject of the information affirmatively places his or her physical or mental condition at issue and the genetic information to be disclosed directly relates to that physical or mental condition.

***Remedies for Unlawful Disclosure or Solicitation of Genetic Information***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York law should be amended to (1) expressly authorize private lawsuits by

victims of unlawful disclosures or solicitations of genetic information against persons who make such disclosures or solicitations and (2) authorize the Attorney General to bring lawsuits on behalf of individuals whose genetic information has been or will be unlawfully disclosed or solicited. In addition, persons and organizations licensed by New York State should be subject to professional discipline for unlawfully disclosing or soliciting genetic information.

- Private and public institutions that deal with genetic information should create their own internal sanctions against persons who unlawfully disclose or solicit genetic information.

***Anonymous Genetic Testing***

- Although anonymous genetic testing has significant drawbacks, it should be an option available to those who desire it. New York law should be amended to eliminate potential barriers to anonymous genetic testing.

## Insurance and Employment

### Insurance

- Currently, insurers do not require applicants to take predictive genetic tests because the tests are very expensive and reveal only a limited number of serious genetic abnormalities. Commentators disagree about whether insurers use genetic information to make adverse insurance decisions. Insurers maintain that they may wish to use genetic information for insurance underwriting in the future.

- Some commentators argue that insurers should be prohibited from using genetic information for insurance underwriting because otherwise individuals, who could potentially benefit from genetic testing, may refrain from undergoing it and thereby endanger their health. Insurers argue that prohibiting the use of genetic information in underwriting could lead to adverse selection and would unfairly favor people who have genetic conditions or identifiable predispositions.

- Some commentators contend that although most Americans appear to consider access to health care a basic right, public attitudes concerning access to life, disability, and long-term care insurance are less clear. These forms of insurance can be seen as means to protect assets rather than as providing access to an important social good, such as medical care. Therefore, according to these commentators, the justifications for prohibiting insurance companies from underwriting using genetic information for these forms of insurance may be less compelling.

- Federal law and the New York Insurance Law prohibit group health insurance plans from making adverse insurance decisions against individuals based on their health status, medical history, and genetic information or from treating genetic information as a pre-existing condition. New York's community rating, open enrollment, and other insurance laws prohibit individual and small group health insurers from making adverse insurance decisions based on genetic information or from treating genetic information as a pre-existing condition.

- Federal law and the New York Insurance Law do not prohibit life, disability, and long-term care insurers from making adverse insurance decisions based on genetic information. However, New York law requires the insurers' decision to be actuarially justified and requires insurers to notify individuals in writing if it charges a higher-than-standard premium or denies an individual insurance based on genetic test results. New York law also prohibits insurers from placing an individual's genetic test results into a nonconsenting relative's records and from drawing, using, or communicating an adverse inference about the relative's genetic status based on these results.

**Employment**

- Commentators disagree over whether employers make adverse employment decisions based on genetic predispositions to disease. Most commentators agree, however, that it is generally inappropriate for employers to fire, refuse to hire, or otherwise discriminate against qualified individuals in the terms and conditions of employment because they have a genetic predisposition to disease.

- Although federal protections against adverse employment decisions based on genetic predispositions to disease are limited, New York law generally prohibits such decisions.

**The Impact of the Americans with Disabilities Act**

- Because it is unlikely that genetic predispositions to disease are "disabilities" within the meaning of the Americans with Disabilities Act, the Act's protections against adverse employment and insurance decisions based on such predispositions are limited.

**Conclusions and Recommendations of the Task Force**

***Health Insurance and Individual Medical Underwriting***

- Access to health care is a necessity for all Americans, and for most Americans, health insurance provides such access. By limiting individual medical underwriting in health insurance, New York's community rating and open enrollment laws appropriately seek to make access to medical care more equitable.

***Current Protections against Adverse Insurance Decisions by Health Insurers Based on Genetic Information***

- The combination of New York and federal laws currently protects New Yorkers from adverse insurance decisions by health insurers based on genetic information.

***Use of Genetic Test Results by Life, Disability, and Long-Term Care Insurers***

- New York insurance law should be amended to require a moratorium on requests for genetic test results and the use of genetic test results in underwriting, by life, disability, and long-term care insurers. Insurers should be permitted to use these results for underwriting only when (1) the subjects of the tests voluntarily provide the results to the insurer and (2) the insurers will use the results for the subjects' benefit.

***Use of Genetic Information by Employers***

- New York Law provides significant protections against adverse use of genetic information by employers. As a result of these protections, it is not necessary to consider further legislation in New York prohibiting the use of genetic information by employers.

## Public Health Role in Genetic Services

- As opposed to clinical medical practice, which focuses on the health of individual patients, public health focuses on disease prevention for whole populations. Public health's core functions include assessment (the systematic collection, assembly, analysis, and dissemination of information about the health of a community), policy development, and assurance of the safety and reliability of, and access to, health services.

- Public health assessment activities in the genetic context include population surveillance and molecular genetic epidemiology research. Policy development activities include the translation of scientific and medical discoveries about genetics into guidelines, regulations, and legislation to promote the public's health. Assurance activities include oversight by the federal government and New York State of genetic testing laboratories.

- New York State has the most far-reaching requirements for genetic test approval and laboratory oversight in the United States. New York State mandates genetic testing laboratories to engage in quality assurance and to employ personnel that meet certain standards. New York also reviews clinical genetic tests for their analytical and clinical validity and requires all laboratories that are located in New York State or test specimens from New York State to obtain a permit for the testing from the New York State Department of Health.

- Commentators have expressed concern about the oversight of predictive genetic testing. They note the current limited degree of federal oversight, the rapid expansion of genetic technologies and clinical genetic tests, and the complexity of genetic test performance and interpretation. Concerns about New York's program of oversight of genetic testing laboratories include disincentives to out-of-state laboratories to participate, timeliness of the program's responses to genetic test approval requests, difficulty locating information about laboratories with New York State permits, and the program's lack of clear criteria for assessing a predictive test's clinical validity.

- The federal and New York State governments, as well as some other states and nongovernmental organizations, promote genetics education for the public and have established and are continuing to establish genetics education programs. The federal and New York State governments also have developed programs to help ensure access to genetic services.

**Conclusions and Recommendations of the Task Force**

***Oversight of Genetic Testing by Federal and State Government Agencies***

- Federal government agencies should strengthen their oversight of clinical laboratory genetic tests, including tests provided as services, to ensure that tests have adequate analytical and clinical validity. New York State should continue its oversight of clinical genetic testing laboratories and should re-examine its criteria and processes for test approval and laboratory oversight.

***Approval Process for Genetic Tests***

- The New York State Department of Health's Laboratory Reference System, and its Clinical Testing Review Panel, should review proposed genetic tests expeditiously, within a specified time period. Approval decisions for individual genetic tests should be made on a case-by-case basis, based on analytical validity and clinical validity data for the test's intended use. The program also should require testing laboratories to provide educational materials to providers ordering the test.

***Establishment of Criteria for Genetic Test Approval***

- The New York State Department of Health should develop clear guidelines to delineate the assessment criteria the Laboratory Reference System will use for approval of genetic tests. The guidelines document should be open for public comment by interested parties, including genetic testing laboratories and clinical geneticists practicing in New York State, prior to adoption by the department.

***State Oversight of Laboratory Quality Assurance***

- The New York Laboratory Reference System should continue to require that permitted genetic testing laboratories meet specified certification, performance, and personnel standards and participate in quality assurance programs.

***Establishment of a Genetic Testing Advisory Committee***

- The New York State Department of Health should create a genetic testing advisory committee, composed of departmental members and representatives of New York's clinical and diagnostic laboratory genetics community, to meet at least annually to review New York's Laboratory Reference System's genetic test approvals, the approval process, and outcomes. The committee also should serve as a sounding board for the clinical genetics and genetic laboratory communities and aid the department in its efforts to disseminate genetic testing information among health care providers.

***Categorization of Approved Genetic Tests***

- For genetic test approval, the New York Laboratory Reference System should move from its current categories of test approval, "generally accepted" and "investigational," to a single category of approved tests in which test-specific limitations or restrictions that are important to patients, providers, and/or payers are noted. For example, approval should specify, when relevant, the need for ongoing data collection to establish a test's clinical validity for its intended application.

***Provider Access to State Oversight Information***

- The New York State Department of Health should ensure that an up-to-date database listing of New York State-approved genetic tests and the laboratories authorized to perform them is readily accessible to health care providers in New York State.

***Exemption from State Regulations for Laboratory Licensure***

- New York's Public Health Law, which requires state licensure for all laboratories performing tests on specimens obtained in New York, should be amended to permit the New York State Department of Health to grant exemptions on a case-by-case basis.

***Ongoing Collection, Evaluation, and Dissemination of Clinical Data***

- Federal and state health agencies should work with laboratories, providers, and other partners to promote the ongoing collection, evaluation, and dissemination of clinical validity and utility data for predictive genetic tests.

***Role of Institutional Review Boards***

- Organizations seeking New York State approval for genetic tests that require ongoing collection of clinical data should be required to submit evidence that they have obtained approval of an institutional review board.

***Assessment of Population Needs***

- Federal and state health agencies play an important role in assessing the population's genetic and environmental risk factors. The New York State Department of Health should continue its activities in statewide assessment of the population's genetic health and genetic epidemiology research.

***Public and Provider Education***

- Federal and state health agencies play an important role in educating the public about genetics generally and about particular genetics services that are available to the public. They also should support production and dissemination of genetics educational materials to health care providers.

***Coordination of State Agency Genetics Activities***

- The New York State Department of Health should assure coordination of activities of departmental personnel and programs that promote genetics health and research activities throughout the department. The department also should promote coordination of its efforts with those of other partners outside the department.

## Integrating Genetics Services into Clinical Care

- Clinical genetics services encompass the application of genetics technology in a wide array of clinical contexts, including treatment and management of genetic disorders and genetic testing for diagnostic and predictive purposes. Genetics services providers include physicians and nurses with special training in genetics, genetic counselors, and others.

- Studies indicate that primary care physicians, who will be utilized for genetic services more frequently as the demands for such services grow, have limited training in genetics and often do not have the knowledge to integrate genetics into primary care services. Commentators have recommended a number of ways to increase genetics

knowledge among physicians, including a greater emphasis on genetics in medical and postgraduate medical training programs, continuing medical education in genetics, and the creation of clinical guidelines for genetic medicine.

- Genetic counselors provide patients with counseling services regarding the occurrence or risk of occurrence of genetic conditions or birth defects. Although no state currently requires genetic counselors to be licensed or certified in order to practice or use the title genetic counselor, genetic counselors can receive board certification from the American Board of Genetic Counselors. In the mid-1990s, about 66 to 75 percent of New York's approximately 150 genetics counselors were board certified.

- Most genetic counselors work in institutional settings as part of a genetics services delivery team and under the supervision of a physician. Under New York law, genetic counselors may not independently order genetic tests for patients. Because there are no specific medical billing codes (CPT codes) for genetic counseling, genetic counselors cannot directly bill third-party payers for the counseling services they provide. Third-party payers do not consider genetic counselors as reimbursable providers in part because the states do not license or certify genetic counselors.

- Increasingly, insurers are covering the costs of predictive genetic testing and counseling for individuals who are at risk for adult-onset disorders or disorders in future offspring. In general, insurers will cover counseling by medical geneticists with M.D. or D.O. degrees, although some insurers will cover counseling by Ph.D. geneticists or nongeneticist physicians.

**Conclusions and Recommendations of the Task Force**

***State Licensure or Certification of Genetic Counselors***

- To ensure an adequate level of competency of genetic counselors and to support the viability of the profession of genetic counseling, New York State should create a process for state certification of genetic counselors who are certified by the American Board of Genetic Counseling or American Board of Medical Genetics.

***Scope of Genetic Counseling Practice***

- Ideally, all genetic counselors should work within a team of health care providers, which may include medical geneticists, Ph.D. geneticists, primary care physicians, and physician specialists, such as oncologists, obstetrician-gynecologists, and neonatologists, to provide genetic counseling as an integrated component of the patient's health care. If genetic counselors practice independently, they should maintain the same level of professional standards as genetic counselors who work within institutional settings and should strive to

achieve the benefits of working in an integrated health care team by consulting with other genetics and nongenetics professionals.

***Authorization to Order Genetic Tests***

- Under New York law, genetic counselors can order genetic testing for their patients only through licensed physicians or other persons who are authorized by law to do so, such as dentists, podiatrists, and nurse practitioners. The Task Force does not recommend any changes to the current law.

***Direct Billing by Genetic Counselors***

- The Task Force encourages the American Medical Association to adopt changes to the CPT codes that would allow nonphysician genetic counselors to bill directly for genetic counseling services.

***Training Genetic Counselors about Legal and Ethical Issues***

- All genetic counselors should receive training in and be knowledgeable about legal and ethical issues relevant to genetic counseling, such as confidentiality and medical privacy. Professional societies of genetic counselors should develop standards and guidelines for educating and training genetic counselors about legal and ethical issues.

***Genetics Training in Medical School and Postgraduate Education***

- Medical schools should incorporate genetics education into their core curriculum. Medical schools and postgraduate training programs should integrate genetics into clinical practice training to teach the necessary skills and attitudes for recognition and assessment of the genetic component of disease.

***Physician Licensure Examinations with Genetics Requirements***

- Physician licensing examinations should assess knowledge of basic genetics issues.

***Genetics Education through Clinical Guidelines***

- Professional medical associations should promote development of comprehensive and up-to-date clinical guidelines to help physicians recognize appropriate genetic testing opportunities, provide a source of continuing genetics education, and ensure that patients receive adequate counseling and appropriate specialty referrals. National and state health agencies and private partners should support the development, updating, and dissemination of professional guidelines.

***Specialty Board Certifications with Genetics Requirements***

- The American Board of Medical Specialties and the individual specialty boards should ensure that specialty board certification and recertification examinations adequately assess genetics competencies.

***Medical Organization-Based Requirements for Genetics Education***

- Managed care and other medical practice organizations should promote genetics education of their member practitioners for the appropriate integration of genetic testing and counseling services and for specialty referrals.

***Genetics Education and Training for Nursing and Allied Health Professionals***

- Nursing and allied health professionals, working with the genetics community, should continue their efforts to incorporate genetics into all levels of nursing practice and allied health services and to promote research to assess and monitor the integration of genetics into all nursing and allied health practices.

# Guide to Abbreviations

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| ABGC | American Board of Genetic Counseling |
| ABMG | American Board of Medical Genetics |
| ABMS | American Board of Medical Specialties |
| ACMG | American College of Medical Genetics |
| ACMGF | American College of Medical Genetics Foundation |
| ACOG | American College of Obstetricians and Gynecologists |
| ADA | Americans with Disabilities Act |
| AMA | American Medical Association |
| ANA | American Nurses Association |
| APC | adenomatous polyposis coli |
| APOE | apolipoprotein E |
| ASHG | American Society of Human Genetics |
| CAP | College of American Pathologists |
| CDC | Centers for Disease Control and Prevention |
| cDNA | complementary DNA |
| CETP | cholesterol ester transferase protein |
| CME | continuing medical education |
| CMV | cytomegalovirus |
| CPT | Current Procedural Terminology |
| CSGC | Cancer Genetics Studies Consortium |
| CVS | chorionic villus sampling |
| DES | diethylstilbestrol |
| DOE | Department of Energy |
| EEOC | Equal Employment Opportunity Commission |
| ELSI | ethical, legal, and social implications |
| ERISA | Employee Retirement Income Security Act |
| FAP | familial adenomatous polyposis |
| FCRA | Fair Credit Reporting Act |
| FISH | fluorescence in situ hybridization analysis |
| HCPCS | Health Care Financing Administration's Common Procedure Coding System |
| HIPAA | Health Insurance Portability and Accountability Act (1996) |
| HMO | health maintenance organization |
| HNPCC | hereditary nonpolyposis colorectal cancer |
| HTLV | human T-cell leukemia virus |
| HuGEM | Human Genome Education Model Project |
| HUGO | Human Genome Organization |
| ICD | International Classification of Diseases |
| IOM | Institute of Medicine |
| IRB | institutional review board |
| ISONG | International Society of Nurses in Genetics |
| IVF | in vitro fertilization |

| | |
|---|---|
| MS | mass spectrometry |
| NAPBC | National Action Plan for Breast Cancer |
| NAS | National Academy of Sciences |
| NBAC | National Bioethics Advisory Commission |
| NCGR | National Center for Genome Resources |
| NCHPEG | National Coalition for Health Professional Education in Genetics |
| NHGRI | National Human Genome Research Institute |
| NIH | National Institutes of Health |
| NSGC | National Society of Genetic Counselors |
| PCR | polymerase chain reaction |
| PGD | pre-implantation genetic diagnosis |
| PKU | phenylketonuria |
| RFLP | restriction fragment length polymorphism |
| TMS | tandem mass spectrometry |

# Glossary of Key Genetic Terms

**Acquired mutation** – a nonheritable, permanent DNA alteration in a cell other than an egg or sperm cell, which may be involved in the development of cancer.

**Allele** – alternative form of a gene (see gene variant).

**Amino acids** – molecules that are the building blocks of proteins.

**Analytical validity** – a measure of how well a laboratory test detects what it is designed to detect, encompassing sensitivity and specificity (see below).

**Autosomal dominant disorder** – a single-gene disorder that results from inheritance of a mutation in a single gene copy.

**Autosomal recessive disorder** – a single-gene disorder that results from inheritance of a pair of genes, both of which have a harmful mutation.

**Carrier –** an individual who has inherited a single, recessive mutant gene variant that is not expressed as a trait or disease. The term carrier is sometimes used more broadly to refer to individuals who have inherited a single mutant gene variant for a dominant trait (e.g., Huntington disease) which has not yet been expressed as disease.

**Chromosome** – rod-like structures located in the cell nucleus that bear a linear array of thousands of genes. Healthy human beings inherit one set of twenty-three chromosomes from each parent.

**Clinical validity** – a measure of a laboratory test's ability to diagnose a disease or predict future disease.

*Clinical utility* ***– a measure of how information learned from a laboratory test enables the person tested to use established preventive, medical, or reproductive options.***

**Congenital disorder** – a disorder present from birth and due to genetic and/or nongenetic factors.

**DNA** – deoxyribonucleic acid; the genetic material of living organisms.

**Gene** – the basic unit of heredity, composed of a linear sequence of DNA bases and coding for one or more specific proteins.

**Gene product** – mRNA or protein molecules specified by a gene.

**Gene variant** (allele) – alternative form of a gene based on variations in DNA base sequence.
**Genetic heterogeneity** – different mutations of a single gene (allelic heterogeneity) or different genes (locus heterogeneity) may be associated with a similar trait or disease.

**Genetic information** – any specific information about variation in form or number of an individual's inherited genes or chromosomes.

**Genetic testing** – analysis of DNA, chromosomes, or gene products that provides specific information about inherited variations in genes or chromosomes of an individual or his or her progeny.

**Genetic screening** – predictive genetic testing targeted to populations to prevent disease and promote health.

**Genotype** – the genetic constitution of all genes of an individual or of a specific gene or genes within an individual.

**Human genome** –the entire array of genes in the human race or of an individual human.

**Inherited susceptibility mutation** – a heritable, permanent DNA alteration that increases an individual's relative risk for a specific condition without guaranteeing that the individual will develop the condition.

**Karyotype** – a photomicrographic display of individual chromosomes, showing their number and structure, which is used to detect inherited chromosomal abnormalities.

**Late-onset testing** – predictive genetic testing to detect inherited gene mutations that cause or increase relative risk for diseases that are not present at birth; generally refers to predictive testing for diseases that occur in adulthood.

**Messenger RNA** (mRNA) –an intermediary molecule that is copied from the DNA sequence of a gene and which carries instructions for the formation of a specific protein.

**Multifactorial disorder** – a disorder that results from multiple causes, both genetic and nongenetic.

**Multiplex testing** – predictive genetic testing for two or more unrelated conditions in a single testing session.

**Mutation** – a permanent change in DNA sequence, resulting from insertion or deletion of one or more bases or from a change in the composition of DNA bases.

**Nucleotide** – DNA or RNA building block; the "letters" of the genetic alphabet.

**PCR –** polymerase chain reaction; a technique by which a specific targeted DNA sequence can be copied million-fold.

**Penetrance** – the probability, based on population data, that inheritance of a specific gene variant by an individual will manifest as a specific trait or disorder.

**Pharmacogenetic testing** – testing for inherited gene variations to guide pharmaceutical drug or other medical treatment to promote positive and prevent adverse reactions.

**Phenotype** – the observable trait expression of a genotype, as influenced by environmental factors.

**Pleiotropy** – property by which a gene influence multiple, seemingly unrelated, traits.

**Predictive genetic testing** – testing to determine inherited variations in form or number of genes or chromosomes by analysis of genes (DNA), gene products (RNA, protein, or specific metabolites), or chromosomes of an individual or an individual's progeny.

**Predispositional testing** — see susceptibility testing.

**Presymptomatic testing** – predictive genetic testing of an asymptomatic person to determine whether an individual has inherited a gene variant (or pair of gene variants) that will result in future disease with almost 100 percent certitude.

**Protein** – large molecules composed of amino acids that form the structural and enzyme components of living organisms. Protein structure is specified by the DNA base sequence of genes.

**Reproductive testing** – predictive genetic testing of an individual, couple, fetus, or pre-implantation embryo to detect heritable genetic disease risks.

*Sensitivity* ***(analytical, clinical) – the ability of a laboratory test to detect all true positive results.***

**Single-gene disorder** (mendelian disorder) – a disorder that results in inheritance patterns following the ratios first described by Gregor Mendel. Inheritance of a single mutated gene variant, or of a pair of mutated gene variants, generally results in a 100 percent disease incidence.

*Specificity* ***(analytical, clinical) – the ability of a laboratory test to exclude from detection all false positive results.***

**Susceptibility testing** (predispositional testing) – predictive genetic testing to detect an individual's inherited disease risk relative to that of the general population.

**X-linked disorder** – a single-gene disorder, generally resulting from inheritance of a single mutant copy of a gene on an X chromosome in a male.

# Introduction

As this report goes to press, the publication of the DNA sequence of the human genome, the three-billion-letter blueprint of human heredity, is imminent. This landmark accomplishment represents the key goal of the Human Genome Project, an international research project launched ten years ago. It will lead, in the next several years, to the identification of the tens of thousands of genes that all human beings share. The Human Genome Project also has promoted development of new analytical technologies that will have a profound impact on both research and health care and will usher in the age of genomic medicine. The long-term benefits of the Human Genome Project will include a better understanding of human health and disease and the development of new pathways for preventing and treating disease. Generally, however, there will be a time lag of years, even decades, between the discovery of the role of a gene in health and disease and the development of interventions that clearly prevent or minimize that risk.

In the meantime, new genomic information and technologies are leading to the development and use of genetic tests to identify inherited variations in human genes that affect a broad range of an individual's health and disease risks. Genetic tests have been used for decades as reproductive tests and as diagnostic tests for persons who display symptoms of some of the several thousand rare "single-gene" diseases such as cystic fibrosis or sickle cell disease — diseases for which the inheritance of one mutated gene, or a pair of mutated genes, leads to a virtually 100 percent disease incidence. As a result of the Human Genome Project, most commentators predict that genetic testing also will be used increasingly to identify future risks not only for rare single-gene diseases but also for common complex disorders of adulthood, including cancer, heart disease, and diabetes. In fact, most chronic diseases are caused by a complex set of both inherited genetic factors, or predispositions, and environmental factors, including diet, lifestyle, and exposure to toxins. The new predictive genetic tests, in addition to identifying persons who are at higher-than-average risk for developing a particular disease, will be able to identify persons who, based on their genetic inheritance, are most susceptible to the harms of exposure to environmental agents, such as cigarette smoke and workplace chemicals. Predictive genetic tests also will be used to guide individual medical treatments, for example, to predict whether an individual is likely to show a favorable or unfavorable response to treatment with a particular pharmaceutical agent.

In the coming decades, human genome research and the development of predictive genetic testing hold enormous promise and, most commentators predict, will lead to a new framework of individualized medicine. With these promises, however, come risks. Many have expressed concerns that the rapid introduction of this new information into health care may harm individuals. These harms may arise from several factors — the lack of preparedness within the health care and clinical laboratory communities for the human genetics research explosion, public misunderstanding of and misperceptions about genetics, and the potential misuses of genetic information against individuals and groups, for example, in insurance and employment. One major concern is that, based on the time

lag between the development of predictive genetic tests and the availability of effective medical interventions, individuals may learn of a future disease risk for which they have no clinically useful options and may experience unnecessary psychological distress.

In the summer of 1997, the New York State Task Force on Life and the Law started a three-year project to address how this wealth of new research data and technologies will affect health care; to identify potential ethical, legal, and social implications; and to propose policy, regulatory, and legislative recommendations to promote the anticipated benefits and avert the risks of genetic testing. The Task Force decided early in its deliberations that it would focus primarily on the predictive uses of clinical genetic testing for heritable genetic variations as the area of most pressing and immediate concern.

In view of the expanding uses of medical genetic information, the Task Force realized that its definition of genetic information and genetic testing must be both precise and broad enough to accommodate future, perhaps yet unanticipated, uses. It wished to avoid the pitfalls experienced by some state legislatures and others that, in the rush to provide special protections for predictive genetic testing, inadvertently established overly narrow guidelines, sometimes with unintended consequences. In this report, we define genetic information as *any specific information about variation in form or number of an individual's inherited genes or chromosomes*. We define genetic testing as *analysis of DNA, chromosomes, or gene products that provides specific information about inherited variations in genes or chromosomes of an individual or his or her progeny*.

The definition of genetic testing used in our report itself encompasses clinical testing performed in different contexts and for different purposes — reproductive testing, diagnostic testing of persons with disease symptoms, predictive testing of healthy individuals to identify future disease risks, and pharmacogenetic testing to guide treatment decisions. Some discussions and recommendations in this report, for example, those to protect confidentiality of genetic information, apply broadly to all forms of genetic testing within our definition. Others apply more narrowly. For example, the recommendations for informed consent to genetic testing apply only to genetic testing used to predict future disease in apparently healthy individuals or their offspring. This form of predictive testing, unlike testing of someone who already has disease symptoms, is often performed solely for informational purposes and may pose significant and avoidable risks.

Another key question the Task Force faced is that of "genetic exceptionalism" — whether and how genetic medicine is different from other areas of medicine and whether genetic testing and information justify special considerations. Task Force members agreed with other commentators who claim that genetic testing is not absolutely different

from other forms of medical testing and that segregating genetic information from other information within a medical record may not be practically feasible. However, members also agreed that predictive genetic testing, notably DNA-based testing, does have some unique characteristics. Predictive DNA-based genetic testing can accurately predict disease risks decades into the future, independent of clinical signs or symptoms, yielding the same specific information about an individual from before birth to after death. It also can amass a uniquely identifiable profile of genetic information for any individual. Other factors that are distinctive, although not always exclusive, to predictive genetic testing include the familial nature of genetic information, poor genetics knowledge and skills in the general health care community, public misperceptions that genetic information is determinative, and a history of using genetics to support discrimination against classes of people, including in the United States. Based on these factors, the Task Force decided that while genetic testing is not absolutely distinct from other medical testing, constellations of factors might merit special concerns about predictive genetic testing in some, but not all, of the areas that the Task Force addressed.

There are two major, and parallel, themes that developed during the course of this project.

> The first is the enormous potential that predictive genetic testing poses for health care and the need to promote utilization of these benefits in both research and clinical care. This led the Task Force to identify barriers to the appropriate uses of genetic testing in research and clinical care and to make recommendations to reduce these barriers. Barriers include concerns about misuse of genetic information in insurance and employment, inadequate genetics knowledge of health care providers, and insufficient oversight of clinical genetic testing laboratories.

The second theme is that, despite the potential promise of predictive genetic testing, there

> are potentially dangerous misunderstandings and misperceptions within the general public about the role of genes in health, disease, and determining who we are as individuals. While it is clear that inherited genetic variations influence an individual's health, disease risks, and even behaviors, many people vastly overestimate the role of genes and underestimate the role of nongenetic, environmental factors. Many also do not adequately appreciate the complexity of interpreting probabilistic genetic information about an individual's risk, relative to that of the general population, for common disorders like breast cancer, heart disease, and diabetes. As we enter the age of genomic medicine, it also is apparent that many health care providers, including most physicians, lack adequate understanding of the role of genetics in health and disease. Public misperceptions, combined with inadequate genetics knowledge of health care providers, could lead people to inappropriately undergo testing, to adopt possibly harmful preventive interventions (or to adopt interventions prematurely), and/or to falsely construe a test result that fails to find a particular gene mutation as meaning that one is at zero risk for future disease. These concerns led the Task Force to make recommendations to promote public and professional education, genetic counseling as part of the informed consent process, oversight of genetics

research using samples obtained in the course of clinical care, and community involvement in policy decisions.

In adopting its focus on predictive genetic testing in the clinical context, the Task Force was unable to consider other important issues beyond this focus. These issues include the conduct of genetics research using tissue samples obtained outside the clinical context; genetic screening for susceptibility to environmental agents in the workplace; genetic testing for acquired, nonheritable gene mutations that may be important in the development and treatment of cancer; genetic testing for behavioral and cognitive traits; somatic gene therapy and reproductive "enhancement"; and the role of private sector research and gene patenting and other commercial factors that may ultimately affect clinical care. The report also does not address issues outside the scope of human genetics and health care, including the use of genomic information about other species to guide antipathogen research, the impact of genetic technologies in agriculture, and the use of genetic profile analysis in law enforcement.

The Task Force offers this report as a guide to policy makers in New York State and elsewhere who are grappling with the difficult issues associated with predictive genetic testing. The Task Force hopes that this report, which includes background information about the science, medicine, and ethical, legal, and social issues of genetics research and clinical practice, will provide a useful and timely educational resource for health care and other professionals and the general public.

# 1

# The Science of Genetics

Genetics is the study of the inheritance of traits. Throughout human history, people have understood that particular traits are shared within families and that similar patterns are observed among animals and plants. In 1865, Gregor Mendel first postulated the concept of genes as discrete biological units responsible for the transmission of specific traits. It was almost a century later, with the 1953 landmark discovery of the structure of DNA, the chemical component of genes,[1] that the field of molecular genetics began. Research about genes and their informational role in heredity has exploded in the succeeding decades, culminating in the initiation of the Human Genome Project in 1990.[2] This international research project to identify all of the estimated 50,000 or so human genes will lead to a much greater understanding of the functions of human genes and their roles in human health and disease.[3]

## The Structure and Function of Genes

The gene is the basic unit of inheritance. Each of the estimated 50,000 human genes acts as a set of instructions for the body to produce one or more specific protein products. Every person has a unique complement of genes, half inherited from the mother and half from the father. Every cell of an individual contains an identical set of genes, located in the cell nucleus.[4]

The chemical building block of genes is DNA. DNA molecules are composed of individual repeated units called nucleotides. Each nucleotide contains an unvarying chemical structure that provides the "backbone" of DNA, as well as one of four distinct chemical bases: adenine (A), cytosine (C), guanine (G), and thymine (T). These four bases provide the letters of the genetic alphabet; their variable positioning along linear

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[1] J. D. Watson and F. H. C. Crick, "Molecular Structure of Nucleic Acids: A Structure for Deoxyribonucleic Acid," *Nature* 171 (1953): 737. See also H. F. Judson, *The Eighth Day of Creation: Makers of the Revolution in Biology,* expanded ed. (Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 1995), 3–169. DNA is an acronym for deoxyribonucleic acid.

[2] U.S. Department of Energy Human Genome Project Information website: *http://www.ornl.gov/hgmis*, visited May 7, 1998.

[3] F. S. Collins, M. S. Guyer, and A. Chakravarti, "Variations on a Theme: Cataloging Human Sequence Variations," *Science* 278 (1997): 1580; L. Rowen, G. Mahairas, and L. Hood, "Sequencing the Human Genome," *Science* 278 (1997): 605; F. S. Collins, "Shattuck Lecture — Medical and Societal Consequences of the Human Genome Project," *New England Journal of Medicine* 341 (1999): 28. As of June 2000, estimates of the number of human genes vary from 30,000 to 100,000. See E. Pennisi, "And the Gene Number Is?" *Science* 288 (2000): 1146; "Editorial: The Nature of the Number," *Nature Genetics* 25 (2000): 127. In this report, we will use the estimate of 50,000.

[4] Almost all human genes are located in the nucleus, but a small number (thirteen, approximately 0.02 percent of human genes) are located in extranuclear structures called mitochondria. See page 9, this chapter.

DNA strands results in specific DNA base "spellings," or sequences.[5] These sequences encode information in the same way that letters of the alphabet form words and sentences.

A gene is a specific DNA base sequence that forms a specific sentence that directs the cell to make a specific protein. The size of individual genes varies from less than 1,000 bases to hundreds of thousands of bases.[6]

### DNA Is Self-Replicating

In cells, DNA exists in double-stranded form. Two single strands of DNA coil around each other to form a structure that looks like a spiraling zipper and is described as a double helix (see Figure 1).[7] The chemical bases of each strand face inside the helix. The interlocking teeth of the zipper are formed by weak chemical bonds between bases of each of the two strands, forming "base pairs." Each base on one DNA strand pairs with a specific base of the other strand; A pairs only with T, and C pairs only with G. This is called base pair complementarity.

This complementarity enables DNA to "copy" its linear base sequence faithfully every time a cell divides to form two daughter cells. During this copying process, called DNA replication, the double-stranded helix "unzips," generating two single-stranded molecules. Each of these single-stranded DNA molecules acts as a template for creation of a new double-stranded helix — individual nucleotides in the cell attach to the single-strand DNA obeying the base-pair complementarity rules. The result is two new double-stranded DNA molecules that are identical to the original (see Figure 2).[8]

### Genes Code for Proteins

The unique base sequence of each gene (its genetic code) directs the cell to produce ("codes" for) one or more specific proteins. Proteins are the major structural and enzyme components of living organisms. The building blocks of proteins are amino acids. There are twenty different amino acids. Each protein contains a unique and characteristic linear array of 100 to 1,000 amino acids, which determines its structure and function.

How does the gene alphabet of DNA's chemical bases convert to the protein alphabet of amino acids? Reading from the start of the gene, each group of three DNA bases, or "triplet," corresponds to a particular amino acid. Conversion of the DNA genetic code to protein, however, is not direct. It requires the participation of an intermediary molecule called mRNA.[9] mRNA is a single-stranded molecule that is

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[5] In the report, we will refer to DNA nucleotide sequences as base or base pair sequences.

[6] M. W. Thompson, R. R. McInnes, and H. F. Willard, *Genetics in Medicine*, 5th ed. (Philadelphia: W. B. Saunders, 1991), 41.

[7] See Appendix B, page 403.

[8] See Appendix B, page 404.

[9] mRNA is an acronym for messenger ribonucleic acid.

similar, but distinct from, DNA. It, too, is composed of long stretches of bases.[10] mRNA molecules are formed on stretches of single-stranded DNA by the same base pair complementarity rules used to make new DNA copies.[11] This process, in which coded genetic information is transferred from DNA to its complementary mRNA, is called transcription.

Once formed, the mRNA strand detaches from its DNA template and moves outside the cell nucleus, where it, in turn, acts as a template for the assembly of a particular protein. This process is called translation. Each mRNA triplet (called a codon) designates insertion of one of twenty amino acids into a linear protein chain. In addition, specific codons located at the end of genes, called "stop" codons, signal the cell that the protein chain is complete.

The transcriptional and translational process in which a gene is "turned on" and copied into mRNA to direct formation of a specific protein is called gene expression. During human development, different groups of cells, all containing the identical set of genes, become "committed" to express particular subsets of genes. For each gene expressed, the number of mRNA (and protein) copies produced also varies. This process of regulated gene expression results in formation of different cell types, tissues, and organs. For example, nerve cells express a subset of genes that encode neurotransmitters and other neuronal proteins, and skin cells express genes that encode specific pigment and fiber proteins.

## Organizational Structure of Genomes and Genes

### *Organization and Replication of the Genome*

The entire DNA content of a cell, an individual, or a species is called a genome. Almost all the DNA of the human genome, over three billion DNA bases, is packaged in discrete units called chromosomes, which are located in the cell nucleus.[12] Long strings of double-stranded DNA, containing genes like beads on a string, are tightly coiled within chromosomes, which provide an organizational structure that allows the controlled copying and segregation of genes each time a cell divides to form two "daughter" cells. During DNA copying or gene transcription to form mRNA, chromosomal DNA temporarily unwinds in a regulated process. A schematic diagram of the cell, showing

[10] In RNA, the base uracil (U) replaces thymine (T); the other three bases (A, C, and G) are identical for DNA and RNA. The chemical "backbone" of RNA nucleotides also differs slightly from that of DNA nucleotides.

[11] For RNA formation, special enzymes cause local breakage of base pair bonds in the gene's double-stranded DNA, creating temporary stretches of single-stranded DNA, like open gaps in a closed zipper. The mRNA molecule forms by stringing of RNA nucleotides together, using the DNA molecule as a template.

[12] The exception is mitochondrial DNA; see page 9, this chapter. Chromosomes also contain special nuclear proteins that aid in DNA "packaging" and the control of gene expression.

chromosomes, their gene constituents, and their location in the cell nucleus, is shown in Figure 3.[13]

Most human cells contain forty-six chromosomes, one set of twenty-three chromosomes derived from the mother and a matching set derived from the father. Egg and sperm cells are the exception, containing a single set of twenty-three chromosomes. Twenty-two chromosomes are called autosomes, and the twenty-third is a sex-determining chromosome, called X or Y.[14] Each of the twenty-two human autosomes and the X and Y chromosomes is unique, containing a specific subset of thousands of genes with a prescribed linear order. The "geographical address" of a particular gene is defined as its locus. For example, the locus of the human beta globin gene is a specific segment of chromosome 11.[15]

When egg and sperm cells unite in fertilization, the resulting fertilized egg contains twenty-two pairs of autosomes and two sex chromosomes (XX in females, XY in males). All cells in the developing human embryo and adult contain the identical set of forty-six chromosomes. Each of the 50,000 genes is present in duplicate copies, one derived from the mother and one from the father. Generally, cells make two copies of any expressed protein, one maternally and one paternally derived.[16]

*Mitosis and Meiosis*

When a cell divides, all the DNA of each chromosome is duplicated. One complete set of chromosomes segregates to each of two new daughter cells. This process is called mitosis. Repeated mitosis and cell division originating from a single fertilized egg generates about 100 trillion cells in a human adult, each with an identical genome.[17] In cells undergoing mitosis, chromosomes are very condensed. This condensed state allows researchers to "stain" cells with chemical agents and examine chromosomes with a microscope. In the resulting chromosome "spread," called a karyotype, researchers can distinguish each of the autosomes and sex chromosomes.[18]

A process similar to mitosis occurs to produce egg and sperm cells. In this process, called meiosis, cells undergo two rounds of division, rather than one. The result

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[13] See Appendix B, page 405.

[14] Each egg cell contains an X chromosome, and each sperm cell contains either an X or a Y chromosome.

[15] Thompson, McInnes, and Willard, *Genetics in Medicine*, 43.

[16] Genes located on the X and Y sex chromosomes are exceptions. In another rare exception, called parental imprinting, the degree to which a gene is expressed varies depending on which parent transmitted it. See R. C. King and W. D. Stansfield, *A Dictionary of Genetics*, 5th ed. (New York: Oxford University Press, 1997), 248.

[17] See "A Brief Key to Basic Genetics," in *Blazing a Genetic Trail*, Howard Hughes Medical Institute website: *http://www.hhmi.org/genetictrail*, visited July 10, 2000.

[18] See also Chapter 2, page 38.

is four rather than two daughter cells, each with only twenty-three (not forty-six) chromosomes.[19] Meiosis also differs from mitosis in another way: Before the first of the two cell divisions, matched pairs of maternal and paternal derived chromosomes line up next to each other — for example, maternal chromosome 1 with paternal chromosome 1, and so on. One or more DNA "breaks" may occur along each of the paired chromosomes and pieces may be "swapped" between the pair. By this process, called recombination, genes originally lined up along the same chromosome can be separated and inherited independently of each other. Thus, individual chromosomes transmitted to offspring are patchworks of the parent's own maternal and paternal chromosomes.

*Noncoding DNA*

Genes, the DNA "sentences" that can be translated into mRNA and then into proteins, comprise about 3 percent of the human genome. An estimated 97 percent of the genome is noncoding DNA.[20] The function of much of the genome's noncoding DNA, if any, is unclear. However, some noncoding DNA sequences are known to regulate the "turning on" and "turning off" of specific genes or chromosomal structure and function.

***Gene Structural Organization***

Most human genes do not contain a continuous, uninterrupted coding sequence; gene "sentences" are interrupted by stretches of noncoding bases, "phrases" of apparent gibberish.[21] When a gene is transcribed into mRNA, both the coding and noncoding stretches of DNA are copied contiguously to produce a long, "immature" RNA molecule. Before protein translation, the cell "edits" the immature RNA, splicing out the noncoding stretches to produce a "mature" mRNA. Although the noncoding DNA stretches of a gene generally do not code for amino acids, they and other noncoding sequences that flank a gene may regulate when, how, and to what level that gene is turned on in the cell.

***Extranuclear Genes: Mitochondrial DNA***

Mitochondria, the "powerhouses" of the cell, are structures outside the cell nucleus that produce energy for the cell's activities. They are the only cell components outside the nucleus that contain DNA. Mitochondrial DNA is a circular double-stranded molecule that contains 16,569 base pairs,[22] coding for thirteen small proteins and for

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[19] At the time of fertilization, each sperm cell has completed meiosis and contains one complete set of twenty-three chromosomes, half the number of other body cells. Egg cells begin meiosis before fertilization but don't complete it until after a sperm cell penetrates its cytoplasm.

[20] See, e.g., R. Weiss and J. Gillis, "Team Finishes Mapping Human DNA," *Washington Post*, June 27, 2000, A01. Most noncoding DNA is made of unique (nonrepetitive) base sequences. The rest is called repetitive DNA and consists of short or long stretches of base sequences that are repeated continuously.

[21] The coding portions are called exons, and the noncoding portions are called introns. Most human genes have exons, from one to over thirty exons per gene, ranging in size from about 100 to 10,000 base pairs. King and Stansfield, *A Dictionary of Genetics*, 182.

[22] Ibid., 216.

special RNA molecules that directly participate in the protein formation machinery.[23] Mitochondrial DNA accounts for a tiny fraction of a cell's entire coding potential, but impairment of this DNA can cause disease.[24] Unlike genomic DNA, mitochondrial DNA is almost exclusively inherited maternally.[25]

### Gene Mutations

Changes in one or more bases within a gene, or the duplication or loss of whole genes, may occur. Often, special DNA repair enzymes in cells correct these errors, but sometimes they go uncorrected and become gene mutations. Mutations may result from errors during DNA copying in dividing cells, or they may occur in "resting," or nondividing, cells, by a reaction with environmental agents (for example, chemicals and radiation) that can modify DNA structure.

Mutations change the "spelling" of a gene sentence. These spelling changes may result from the addition of one or more incorrect bases (substitution mutations), insertions of one or more additional bases (insertion mutations), or the loss of one or more bases (deletion mutations). Alteration of a single base within a gene, called a point mutation, can change a single mRNA codon and result in insertion of a single altered amino acid within a protein. If the mutation changes the codon to one of several "stop" codons that function to stop protein production, the gene can no longer produce a normally sized protein.

Other types of mutation also can alter the genetic code. Deletion or insertion of one or more bases disrupts the framework in which contiguous DNA base triplets are read. This causes the whole sequence of mRNA codons to fall out of line and results in production of a partial, generally nonfunctional, protein.[26] Another type of mutation is called a trinucleotide repeat expansion. Trinucleotide repeats are unstable DNA regions in which particular nucleotide triplets (for example, CAG) occur as multiple repeats (CAGCAGCAGCAG . . . ). Normally the triplet sequence repeats five to fifty times, but mutation can expand the number of repeats, generating up to hundreds or thousands.[27] This type of mutation is involved in many human neurological disorders.[28]

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[23] These forms of RNA, called tRNA and rRNA, are related to but distinct from mRNA. tRNA and rRNA do not act as transcriptional intermediates between gene and protein.

[24] See P. F. Chinnery and D. M. Turnbull, "Mitochondrial DNA and Disease," *The Lancet* 354 suppl. I (1999): 17. See also page 20, this chapter.

[25] See page 20, this chapter.

[26] For example, in a hypothetical gene sequence reading "GACTACGATTCT . . ." DNA base triplets corresponding to mRNA codons would be "GAC-TAC-GAT-TCT . . ." If the second base (A) is deleted, the triplet framework changes to "GCT-ACG-ATT-CT . . ." changing the encoded amino acids. The new triplet ATT corresponds to one of several mRNA "stop" codons that direct the cell to terminate protein production.

[27] King and Stansfield, *Dictionary of Genetics*, 350.

[28] See page 16, this chapter.

Not all gene mutations, however, change the genetic code. Mutations within the noncoding stretches of genes generally do not affect encoded proteins. Also, in some cases, base changes within the coding DNA will not change the amino acid composition of the encoded protein.[29] If the mutation has no apparent effect on the encoded protein, it is called a silent mutation.

More extreme types of mutation also can occur: change in gene number (e.g., gene duplication), chromosome number, or chromosome structure. These abnormalities characteristically occur during mitosis or meiosis. For example, during chromosome copying and cell division, if two matching, newly copied chromosomes fail to move away from each other into two new daughter cells, one of the daughter cells will lack a chromosome and the other daughter cell will have an extra chromosome.

A mutation in an egg or sperm cell is transmissible to future generations and is called a heritable, or germline, mutation. Heritable mutations that block the production of a normal protein may alter traits or cause disorders. Mutations that occur in cells other than egg and sperm cells, called acquired, or somatic, mutations, are not heritable. These mutations play a key role, however, in the generation of most human cancers. Cancer is the result of successive mutations in several key genes in a single cell, usually over many decades. These cumulative mutations progressively impair the regulation of the cell's growth properties, creating a malignant clone of cells.[30]

## Genetic Inheritance and Diversity

Heritable mutations account for the generation of alternative forms of a gene within the population. The alternative forms of a specific gene are called alleles; this report will use the term "gene variants."[31] The specific DNA sequence of each gene variant is called its genotype.[32] The expression of a particular genotype by a cell or an individual is called a phenotype, or trait.[33]

Every individual has a unique genome, resulting from a combination of maternal and paternal chromosomes. Every individual has two copies of every gene. For any specific gene, the inheritance of two copies (for example, for blue versus brown eye

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[29] There are sixty-four possible triplet codons (using the four DNA/RNA base combinations) and only twenty amino acids. Commonly, variations in the third base of a codon will not alter the coded amino acid.

[30] American Cancer Society, *Cancer and Genetics — Advising Your Patient's Relatives* (Huntington, NY: PRR, 1997), 32–34. See also page 19, this chapter.

[31] In population genetics, alternative forms of genes are caused by variations in DNA sequence detected by an effect on trait expression or by DNA sequencing analysis. When referring to individuals, the term allele also is used to distinguish the two genes at a given locus (one inherited from the mother and the other from the father). This report will also use the term gene variants to refer to alleles. In the popular press, some use the term gene mutation or mutation to refer to particular alleles that are associated with disorders.

[32] A genotype is the genetic constitution of all genes of an individual or of a specific gene or genes within an individual.

[33] A phenotype is the observable trait expression of a genotype, as influenced by environmental factors.

pigment) affects variation in traits.[34] Within an individual, the maternal and paternal copies of a specific gene may be identical (e.g., blue/blue). Alternatively, they may be different (e.g., blue/brown).

Scientists estimate that individuals differ in approximately 1 in 300 to 1,000 base pairs of DNA.[35] Within the human population, there may be hundreds of variants for any particular gene, although for many identified genes, two or three common population variants have been characterized;[36] these are called polymorphic genes.[37] An example of a polymorphic human gene is the gene that determines ABO blood types; inheritance of one or two copies of three different variants of this gene, A, B, and O, determines blood type.[38]

**Mendelian Gene Inheritance**

In 1865, Gregor Mendel, an Austrian monk experienced in horticulture and educated in physics, outlined the basic principles of genetic inheritance.[39] These concepts, known as Mendel's laws, resulted from his breeding experiments with garden peas. In agriculture, breeders had long recognized patterns of inheritance but could not understand their basis. For example, some traits skipped generations or disappeared. Mendel's experiments explained these phenomena by the following principles:

- Genes are inherited as discrete, indivisible units,[40] in matching pairs, one from each parent. Inherited gene pairs do not blend but retain their identity, and traits not expressed in one generation may reappear in the next.

- Maternal and paternal copies of each gene segregate from each other when passed to the next generation.

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[34] In humans, eye color is a complex trait determined by more than a single gene.

[35] Collins, "Medical and Societal Consequences of the Human Genome Project," 32; M. Hagmann, "A Good SNP May Be Hard to Find," *Science* 285 (1999): 21; C. Cantor, "How Many SNPs Are Enough?" *GeneLetter* (March 2000), GeneLetter website: *http://www.geneletter.com*, visited March 28, 2000; Thompson, McInnes, and Willard, *Genetics in Medicine*, 127.

[36] E. S. Lander, "The New Genomics: Global Views of Biology," *Science* 274 (1996): 536, 537.

[37] A gene is polymorphic when at least two variants of the gene appear within a defined population group with frequencies greater than 1 percent.

[38] The A, B, O blood group polymorphism, the first human genetic polymorphism described in 1900, is caused by a few single base variations and is associated with slightly modified versions of a specific protein on the surface of red blood cells. See A. Schafer and R. Hawkins, "DNA Variation and the Future of Human Genetics," *Nature Biotechnology* 16 (1998): 33.

[39] W. Bodmer and R. McKie, *The Book of Man — The Human Genome Project and the Quest to Discover Our Genetic Heritage* (New York: Oxford University Press, 1994), 15.

[40] Mendel postulated unit inheritance by genes and alleles, but these terms did not come into use until decades later. For discussion of Mendel and his work, see Bodmer and McKie, *Book of Man*, 14–17.

- Inheritance of a particular trait from one parent is not usually linked to inheritance of an unrelated trait from that parent.[41]

Mendel introduced the concept of dominance and recessiveness of gene variants for specific traits. In the expression of a specific simple plant trait (e.g., stem length), one of the two inherited copies of the gene controlling that trait could dominate the other — for example, the variant for long stems could dominate, or mask, the variant for short stems. The masked, or recessive gene copy, in this case, for short stems, must be present in two copies for the trait to be expressed — in this case, a short-stemmed plant. For some genetic traits, however, gene variants also may be codominant, with both of them fully contributing to the trait. An example is codominance for a gene controlling flower color in some plants. Breeding a white flower with a red one would produce a flower with one gene copy for white pigment and the other for red pigment, resulting in a pink flower.[42]

**Human Genetic Traits and Disorders**

Mendel's laws are universal and operate for all plants, animals, and humans. For observers of human inheritance, however, simple genotype-phenotype correlations seen for Mendel's pea plants are rare. Generally, most human traits are less simple and are influenced by multiple genes. This is true even for basic physiological traits such as eye color and height. Environmental factors also influence trait expression, even for so-called single-gene traits and disorders.[43] Environmental factors include prenatal conditions and postnatal diet, lifestyle, and exposure to radiation and chemicals.

***Variable Aspects of Trait Expression***

It is often difficult to predict how a particular inherited gene variant will be expressed. There are several complexities of gene expression that affect trait expression:

- Incomplete Penetrance — Penetrance is the probability, based on population data, that inheritance of a specific gene variant by an individual will manifest as a specific trait or disorder. Some gene variants that cause disorders have 100 percent penetrance, but many others show incomplete penetrance. For example, inheriting a mutation in a gene called BRCA1 increases lifetime risk for breast and ovarian cancer but does not guarantee a person will develop cancer.[44]

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[41] The exception to this rule is for genes that are very close to each other on the same chromosome and unlikely to be separated by recombination during meiosis. See page 9, this chapter.

[42] In this example, a white flower has two w (w/w) copies of the gene that codes for pigment, and a red flower has two r (r/r) copies of the same gene. When crossed, all resulting flowers would have one w and one r copy (w/r) of the gene, resulting in pink color.

[43] A disorder is defined as a disturbance of function, structure, or both, resulting from a genetic or embryologic failure in development or from exogenous factors such as poison, trauma, or disease. *Stedman's Electronic Medical Dictionary* (Philadelphia: Williams and Wilkins, 1995).

[44] See Chapter 3, page 63.

- Variable Expressivity — This concept relates to the range of trait (or disorder) expression in an individual. Different individuals who inherit the same gene variant, even those within the same family, may show variable symptoms and disease severity. For example, children with sickle cell disease show variable range and severity of symptoms.

- Variable Age of Onset — Many genetic disorders are late-onset, manifesting at some time after birth, often in adulthood, and onset cannot be predicted precisely. Huntington disease, caused by inheritance of a mutation in a single gene, generally does not develop until middle age.[45]

- Allelic Heterogeneity — Within populations, there may be many different variants of a particular gene caused by different possible mutations within that gene. Different mutations in the different variant forms of the gene may result in the same abnormal trait or disease. For some large genes, hundreds of different mutations can cause the same disease. An example is cystic fibrosis.[46]

- Locus Heterogeneity — Mutations in one of several different genes could cause or contribute to the development of the same disease. The same symptom or disorder could be caused by the inheritance of a mutation in one of several genes. One form of familial colon cancer is caused by the inheritance of a mutated copy of one of several genes that have similar function.[47]

- Pleiotropy — A single gene is often responsible for a number of distinct and seemingly unrelated traits.[48] In humans, different variants of a gene called apolipoprotein E (APOE) affects cardiovascular disease risk and also may affect risk for developing late-onset Alzheimer disease.[49]

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[45] See page 16, this chapter; see also Chapter 3, page 61.
[46] See Chapter 5, page 117. See also Chapter 2, page 42.
[47] This form of familial colon cancer, called HNPCC (hereditary nonpolyposis colon cancer), accounts for about 3 percent of colon cancers. See Chapter 3, page 66.
[48] King and Stansfield, *Dictionary of Genetics*, 264; R. E. Pyeritz, "Pleiotropy Revisited: Molecular Explanations of a Classic Concept," *American Journal of Medical Genetics* 34 (1989): 124. For further discussion, see Chapter 3, page 76.
[49] See Chapter 3, page 67.

### *Single-Gene Traits and Disorders*

Single-gene traits and disorders were the focus of the earliest human genetic studies because of their simple inheritance patterns. One example, frequently used in school biology classes, is the ability or inability to roll (or curl) one's tongue, side to side. The ability to roll the tongue is dominant. Another, more medically relevant example, is the ABO blood group system. There are three major population variants of a single gene, one recessive variant (O), and two codominant variants (A and B). Knowledge of parental ABO blood type (and, by inference, the underlying genotypes) may be sufficient to predict the incidence of ABO blood types in the next generation.[50]

Some human gene disorders show a very high, sometimes 100 percent, concordance with inheritance of a particular gene variant — these variants are said to be 100 percent penetrant. These disorders, called Mendelian or single-gene disorders, generally segregate within families according to Mendel's laws. Transmission of a particular mutated gene variant associated with a disorder can be mapped over family generations. Resulting diagrams, called pedigrees, can be used to predict the probability that additional individuals within a family will be affected. Although the term implies that a gene dictates a disease process alone and directly, other genetic and nongenetic factors account for the variable expressivity and age of onset that is characteristic of many so-called single-gene disorders.

Beginning in the early 1900s, efforts by genetically trained physicians to determine the genetic roots of human disease generated a catalogue of disorders that show Mendelian inheritance. Several thousand single-gene disorders have been described, but their overall population incidence is low.[51] These genetic disorders are grouped in three categories, based on the chromosomal location of the mutant gene variant (autosomal versus sex chromosome) and their mode of inheritance (dominant versus recessive). The categories are autosomal dominant, autosomal recessive, and X-linked.

### *Autosomal Dominant Disorders*

Autosomal dominant disorders result from inheritance of a single mutant gene variant located on any of the twenty-two autosomal chromosomes. In a pedigree, children of an affected parent have a 50 percent chance of inheriting the disorder. Males and females are equally likely to transmit and to inherit a disorder. More than half of identified single-gene disorders are characterized as autosomal dominant.[52] Examples include adult polycystic kidney disease, familial hypercholesteremia, neurofibromatosis, and Huntington disease.[53]

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[50] For example, since the O variant is recessive, type O parents have two copies of the O variant and their children will also all be type O. If one parent is type AB (AB) and one is type O (OO), the children can inherit either an A and an O (type A blood) or a B and an O (type B blood).

[51] Incidence varies for different disorders and populations. In the United States, the incidence of individual single-gene disorders ranges from about 1 in 1,000 to one in several tens, or hundreds, of thousand births. Thompson, McInnes, and Willard, *Genetics in Medicine*, 5–7. Synopses of these disorders have been compiled in a website tool, the Online Mendelian Inheritance in Man website: *http://www.ncbi.nlm.nih/gov/Omim*, visited August 8, 2000.

[52] T. D. Gelehrter, F. S. Collins, and D. Ginsburg, *Principles of Medical Genetics*, 2d ed. (Baltimore: Williams and Wilkins, 1998), 24.

[53] In this report, the possessive "s" is not used for disorders named by eponym (for example, Huntington's disease), following V. McKusick, "Commentary: On the Naming of Clinical Disorders, with Particular Reference to Eponyms," *Medicine* 77 (1998): 1.

Huntington disease, a progressive neurological disorder, is a classic example of an autosomal dominant disease. George Huntington described the disease in 1872 and called it Huntington's chorea, due to the dance-like, shaking movements of affected individuals. The disease is a devastating one, marked by progressive mental and neurological deterioration over one or two decades. Symptoms do not begin until late midlife, after many individuals have had children.[54]

The disease affects approximately 1 in 20,000 individuals.[55] The gene associated with the disease was discovered in 1993. The disease is caused by a trinucleotide repeat expansion mutation within this gene;[56] generally, individuals who inherit a mutated gene variant have a 100 percent chance of developing Huntington disease.[57]

*Autosomal Recessive Disorders*

In the early 1900s, A. E. Garrod, an English physician, postulated that some human disorders followed Mendel's rules for inheritance of recessive alleles. He noted that some rare conditions were present at birth in two or more siblings of unaffected parents. Thus, the parents were "carriers"[58] of a trait that they themselves did not express; each parent "carried" one mutant gene copy and one normal copy. Affected children inherited two mutant copies of the gene. Garrod called these disorders "inborn errors of metabolism" and postulated correctly that children with these disorders had inherited two defective copies of a gene encoding a critical enzyme.[59]

The patterns of inheritance observed by Garrod are characteristic of autosomal recessive disorders; the appearance of the disorder within a family is often sporadic, both parents appear healthy and unaffected, one in four children manifests the disorder, and male and female children are at equal risk.[60] These disorders account for approximately 36 percent of single-gene disorders.[61] Their overall incidence is relatively rare but may be

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[54] Age of onset varies from the third to the seventh decade; it usually manifests in the fifth decade.

[55] Gelehrter, Collins, and Ginsburg, P*rinciples of Medical Genetics*, 217.

[56] See page 10, this chapter.

[57] American College of Medical Genetics/American Society of Human Genetics Huntington Disease Genetic Testing Working Group, "Laboratory Guidelines for Huntington Disease Testing," *American Journal of Human Genetics* 62 (1998): 1243, 1244.

[58] A carrier is defined as an individual who has inherited a single, recessive mutant gene variant. King and Stansfield, *Dictionary of Genetics*, 50. The term carrier also may be used more broadly to refer to individuals who have inherited a single mutant gene variant for a dominant trait that has not been expressed, e.g., for an individual presymptomatic for Huntington disease. See Thompson, McInnes, and Willard, *Genetics in Medicine*, 428.

[59] H. E. Sutton, *An Introduction to Human Genetics*, 2d ed. (New York: Holt, Rinehart and Winston, 1975), 5; A. E. Garrod, "Inborn Errors of Metabolism," *The Lancet* 2 (1908): 1.

[60] Statistically, for children of two carriers, 25 percent will inherit two copies of the mutant gene, 25 percent will inherit two normal copies, and 50 percent will be healthy carriers of a single mutant copy.

[61] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 24.

significantly elevated in certain population groups. Autosomal recessive diseases that have elevated incidences within particular population groups in the United States include cystic fibrosis, sickle cell disease, and Tay-Sachs disease. Cystic fibrosis affects 1 in 2,000 Caucasians, sickle cell disease affects 1 in 400 African Americans, and Tay-Sachs disease affects 1 in 3,600 births in the Ashkenazi Jewish population.[62]

*X-Linked Disorders*

In X-linked (or sex-linked) disorders, healthy mothers carry a mutant gene variant on one of their two X chromosomes. Generally, the presence of a second, normal copy of the same gene on the mother's other X chromosome is sufficient to prevent disease. Carrier mothers have a 50 percent chance of transmitting the mutant gene variant to each son and daughter. When transmitted, daughters, similar to their mothers, are healthy carriers. However, sons who inherit only the mutant gene copy are subject to the disorder.[63] X-linked disorders account for approximately 10 percent of single-gene disorders.[64] An example is hemophilia, a blood-clotting disorder caused by an inability to produce a normal blood coagulation protein called factor VIII. Hemophilia affects approximately 1 in 10,000 male infants.[65] In the nineteenth and early twentieth centuries, hemophilia afflicted the royal houses of Europe, originating with Queen Victoria, a carrier.[66]

Some cite hemophilia as the first recorded human genetic disease. Over 1,500 years ago, Talmud scholars directed that when a boy within a family died from excessive bleeding following circumcision, later sons of that mother *and sons of her sisters* need not be circumcised.[67] This directive recognized not only the carrier status of the mother of the affected boys but also the high probability (50 percent) that her sisters also were carriers.

***Multifactorial Disorders***

Almost all human diseases are thought to be at least partially genetic, including common complex disorders such as cancer, heart disease, diabetes, and psychiatric illnesses.[68] Even susceptibility to infectious diseases is affected by genetics.[69] Although

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[62] Ibid., 4. However, because of carrier screening programs initiated in the early 1970s and the development of prenatal testing for Tay-Sachs disease, the incidence of Tay-Sachs births within the Ashkenazi Jewish community has declined steeply. See Chapter 5, page 113.

[63] Thompson, McInnes, and Willard, *Genetics in Medicine*, 78.

[64] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 24.

[65] Thompson, McInnes, and Willard, *Genetics in Medicine*, 76.

[66] Bodmer and McKie, *Book of Man*, 8–9.

[67] H. E. Sutton, *An Introduction to Human Genetics*, 2; American Cancer Society, *Cancer and Genetics*, 74.

[68] F. S. Collins, "Afterward: The Impact of the Human Genome Project on Medical Practice," in *Toward the 21st Century: Incorporating Genetics into Primary Health Care*, ed. N. Touchette et al. (Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 1997), 87.

[69] This includes susceptibility to the HIV virus. See M. W. Smith et al., "Contrasting Genetic Influence of CCR2 and CCR5 Variants in HIV-1 Infection and Disease Progression," *Science* 277 (1995): 959.

inheritance of specific gene variants may significantly increase risk for particular disorders, the influence of inheritance is generally too complex for construction of simple pedigrees. Those gene variants that contribute a significant increase in disease risk are called inherited susceptibility mutations.[70] Whether or not a person who inherits a susceptibility mutation will get a particular disease depends on other genes that person inherits and also on his or her lifetime environmental exposures. These mutations predispose individuals to disorders; they range from weakly to strongly penetrant.

Late-onset Alzheimer disease, affecting approximately four million Americans, is a multifactorial disease.[71] Alzheimer disease occurs at a higher than general incidence within some families, but patterns are significantly more complex than for single-gene disorders. For example, APOE, a gene that codes for a protein that influences blood cholesterol levels, is associated with increased risk for late-onset Alzheimer disease in Caucasians.[72] The APOE locus has three common population variants, of which one, E4, is linked to increased risk for Alzheimer disease. In studies involving Caucasian populations, inheritance of one copy of the E4 variant, about a quarter of that population,[73] approximately doubles lifetime Alzheimer disease risk,[74] from a general population risk of about 15 percent.[75] Inheritance of two copies of the APOE4 variant, about 2 to 3 percent of the Caucasian population,[76] poses a higher lifetime relative risk for the disease.[77]

While this increased risk is significant, inheritance of an E4 variant of the APOE gene is neither necessary nor sufficient to cause Alzheimer disease.[78] Other factors influence disease incidence, including other "risk" genes and environmental factors.[79]

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[70] N. A. Holtzman, "Scale-Up Technology: Moving Predictive Tests for Inherited Breast, Ovarian, and Colon Cancers from the Bench to the Bedside and Beyond," *Journal of the National Cancer Institute Monographs* 17 (1995): 95.

[71] C. L. Lendon, F. Ashall, and A. M. Goate, "Exploring the Etiology of Alzheimer Disease Using Molecular Genetics," *Journal of the American Medical Association* 277 (1997): 825.

[72] R. Mayeux and N. Schupf, "Apolipoprotein E and Alzheimer's Disease: The Implications of Progress in Molecular Medicine," *American Journal of Public Health* 85 (1995): 1280; O. Kosunen et al., "Relation of Coronary Athlerosclerosis and Apolipoprotein E Genotypes in Alzheimer Patients," *Stroke* 26 (1995): 743; see also Chapter 3, page 67.

[73] L. M. McConnell et al., "Genetic Testing and Alzheimer Disease: Has the Time Come?" *Nature Medicine* 4 (1998): 757, 758.

[74] M. Morrison-Bogorad, C. Phelps, and N. Buckholtz, "Alzheimer Disease Comes of Age: The Pace Accelerates," *Journal of the American Medical Association* 277 (1997): 837.

[75] S. G. Post et al., "The Clinical Introduction of Genetic Testing for Alzheimer Disease: An Ethical Perspective," *Journal of the American Medical Association* 277 (1997): 832.

[76] Mayeux and Shupf, "Apolipoprotein E and Alzheimer Disease," 1281; McConnell et al., "Genetic Testing and Alzheimer Disease," 758.

[77] Morrison-Bogorad, Phelps, and Buckholtz, "Alzheimer Disease Comes of Age," 837. Based on some studies, individuals with two copies of the APOE4 variant have a 5.1- to 17.9-fold increased risk.

[78] Mayeux and Shupf, "Apolipoprotein E and Alzheimer Disease," 1281.

[79] Morrison-Bogorad, Phelps, and Buckholz, "Alzheimer Disease Comes of Age," 837; D. L. Price, S. S. Sissodia, and D. R. Borchelt, "Alzheimer Disease — When and Why," *Nature Genetics* 19 (1998): 314.

### *Inherited Cancer Susceptibility Mutations*

Cancer results from acquired gene mutations and can be considered a multifactorial genetic disorder.[80] Scientists have discovered three types of genes that, when mutated, predispose a cell to cancer.[81] The first type, oncogenes, encode for proteins whose normal function is to accelerate cell growth. Mutated oncogenes act dominantly to keep the cell continually dividing. The second type, tumor suppressor genes, code for proteins whose normal function is to act as "brakes" on cell growth and division. Mutant tumor suppressor genes work in a recessive fashion. The mutant phenotype (lack of cell brakes) manifests only when both copies of the gene are affected, resulting in no functional protein. The third type, DNA repair genes, code for proteins that act as the cell's "proofreaders" for newly copied DNA every time a cell divides. A mutation that impairs one of the cell's DNA proofreaders increases the chance that new mutations in other cancer-related genes will go uncorrected and a cell will become cancerous.

In a minority of cancers, the first mutation that starts the process of cell deregulation is inherited. Approximately twenty highly familial cancer syndromes have been described. In some cases, inheritance of identified gene mutations pose a 100 percent risk of cancer; one example is a rare form of familial colon cancer.[82] In other cases, inheritance of a familial susceptibility mutation increases cancer risk but does not guarantee that a person will develop cancer.[83] All the cells of individuals who inherit these susceptibility mutations have taken a first step toward cancer, but additional mutations must occur before any cell becomes cancerous.[84]

An example of a strong familial cancer susceptibility mutation is a mutant gene variant of the breast cancer susceptibility 1 (BRCA1) gene. Inheritance of a mutant BRCA1 gene variant increases lifetime risk of breast and ovarian cancer in women but does not always result in cancer.[85] For any cell to become cancerous, mutation of the second (normal) BRCA1 gene copy and other genes must occur. Moreover, inheritance of the same mutant variants of the BRCA1 gene within different families confers different degrees of risk.[86] This difference reflects the influence of other inherited genes and environmental factors in the development of breast cancer.

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[80] See page 11, this chapter.
[81] American Cancer Society, *Cancer and Genetics*, 32–33.
[82] This form of colon cancer is called familial adenomatous polyposis (FAP). For a discussion, see Chapter 2, page 44; see also Chapter 8, page 222.
[83] It is estimated that 5 to 10 percent of cancers show some familial inheritance. National Cancer Institute, *Understanding Gene Testing*, NIH Publication No. 97-3905 (Bethesda, MD: National Institutes of Health, 1997), 12, and National Institutes of Health website: *http://www.rex.nci.nih.gov/PATIENTS/ INFO_TEACHER/bookshelf/ NIH_gene_testing/gene00.html*, visited July 7, 2000.
[84] American Cancer Society, "Cancer and Genetics," 32–34.
[85] See Chapter 3, page 64.
[86] B. Healy, "BRCA Genes — Bookmaking, Fortune-Telling, and Medical Care," *New England Journal of Medicine* 336 (1997): 1448. A woman with a strong family history of breast or ovarian cancer, or both,

### *Chromosomal Disorders*

During meiosis and mitosis, errors in chromosomal recombination or segregation can result in chromosomal aberrations. There are two types of chromosome disorders: changes in the number of chromosomes, called aneuploidy, and chromosome translocation.[87] Translocation results from transfer of a chromosome segment, usually containing many genes, onto another part of the same or another chromosome. When unbalanced translocation of chromosomal segments occurs during meiosis, one daughter cell gains an extra chromosomal segment, and another daughter cell loses that segment. Chromosomal aberrations often occur spontaneously in families and generally result in significant developmental abnormalities.

Chromosomal disorders also are called cytogenetic disorders. They are often severe enough to spontaneously terminate fetal development; half of first trimester spontaneous abortions are attributed to chromosomal disorders.[88] Over sixty identified chromosomal disorders are collectively more common than single-gene disorders, affecting 7 in 1,000 live births.[89] These include Down syndrome, also called trisomy 21, which results from inheritance of an extra copy of all or specific portions of chromosome 21.[90]

### *Mitochondrial Gene Disorders*

Mitochondrial DNA accounts for a tiny percentage of the cell's DNA coding instructions, but some genetic disorders are associated with mutant mitochondrial genes. Since mitochondria are not in the cell nucleus, the inheritance pattern of a mutant mitochondrial gene is distinct from those discussed earlier.[91] During fertilization, the sperm contributes only nuclear material. Generally, all extranuclear components, including mitochondria, derive completely from the egg. As a result, transmission of mitochondrial DNA is from mother to children of both sexes; there is no paternal contribution. An example of a mitochondrial gene disorder is Leber disease, a rare maternally inherited disease that results in blindness in young adults.[92]

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who has an inherited BRCA1 mutation has an 85 percent lifetime risk of developing breast cancer. BRCA gene mutations may confer a lower lifetime risk for women outside these families. For a discussion, see Chapter 3, page 64.

[87] See Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 162–169.

[88] Ibid., 169.

[89] Thomas, McInnes, and Willard, *Genetics in Medicine*, 7, 21.

[90] Ibid., 219–221.

[91] See Chinnery and Turnbull, "Mitochondrial DNA and Disease"; see also page 10, this chapter.

[92] A. Soumalainen, "Mitochondrial DNA and Disease," *Annals of Medicine* 29 (1997): 235.

## Gene Discovery and the Human Genome Project

### Gene Discovery

Since the 1980s, researchers have used the tools of molecular biology to identify human genes and genes of other animals species, including fruitflies and mice, to study the role of specific genes in health and disease. The basic technique of molecular biology used is called DNA cloning, in which scientists isolate a copy of a particular segment of DNA, such as a specific gene, and copy that particular DNA segment millions of times, generating a pure and reproducible source.[93] Once isolated in pure form, researchers can analyze the base sequence of the cloned DNA and use normal and modified versions of a cloned gene in functional studies.

#### *Functional Gene Cloning*

The oldest approach to gene identification is functional gene cloning, in which researchers start by identifying key proteins involved in a physiological process of interest. Once researchers identify a specific protein, they can isolate it and analyze its amino acid composition. From this amino acid sequence information, researchers can work "backwards" to deduce the gene sequence and then scan for that sequence in the genome.

#### *Positional Cloning*

Researchers also have used an approach called positional cloning to identify human genes that, when mutated, result in single-gene diseases such as cystic fibrosis and Huntington disease. This approach is based on use of human chromosome "maps" that identify thousands of DNA markers that can be distinguished among different individuals in a population. These gene discoveries have resulted from years of painstaking research, generally involving large families and population groups that are at special risk for specific heritable disorders.[94]

In this approach, researchers collect blood samples from affected and unaffected family members and test them for hundreds of identified DNA markers that map to all twenty-four chromosomes, looking to see if one or more markers are co-inherited with the

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[93] For DNA cloning, researchers start with a purified DNA preparation (e.g., a preparation of genomic human DNA prepared from a blood sample). They cut the long DNA strands into fragments of several hundred to several thousand bases long and combine the mixture with another source of cut DNA, known as vector DNA. Vector DNA is a special type of DNA that normally undergoes million-fold replication when reintroduced into its normal host cell, commonly bacteria. In cloning, the inserted human DNA fragments are copied along with the vector; specific fragments of interest can be isolated in relatively high copy number and pure form. A set of clones containing all DNA fragments of an individual genome is called a genomic library.

[94] For a discussion, see B. Merz, "Kinships That Hold Clues to Disease," in *Blazing a Genetic Trail*, Howard Hughes Medical Institute website: *http://www.hhmi.org/genetictrail*, visited July 10, 2000; see also Chapter 2, page 36.

disorder. If so, researchers can map the gene for the disorder to that region, using computer-aided analysis. When the chromosomal position is narrowed sufficiently, researchers can target a specific stretch of DNA for sequence analysis and identify the gene of interest that is linked to the marker. Positional cloning has identified genes associated with over 100 highly penetrant gene disorders, including Huntington disease and cystic fibrosis.[95] In the last several years, as the Human Genome Project generated progressively greater numbers of DNA markers, the positional cloning approach has become faster and easier. Whereas positional cloning of the CFTR gene, associated with cystic fibrosis, required about 100 researchers and ten years, a more recent discovery of another single-gene disease-associated gene required only a few researchers and a single year.[96]

## *Animal Models*

For human gene discovery and analysis, scientists also can use various animal models, including mice. The mouse genome is very similar to the human genome, containing mouse homologues (related copies) for most human genes.[97] For decades, researchers have derived "strains" of mice that are virtually genetically identical to each other by a process of brother-sister matings over many generations. Mice live only two to three years and female mice can produce multiple litters of up to ten baby mice each, with each pregnancy lasting only about twenty days. These factors allow researchers to identify and analyze the role of specific genes in mice more easily than in humans.[98]

Animal models also provide a way for researchers to perform gene modification experiments that would not be possible in humans. For the last two decades, researchers have been able to genetically modify a targeted gene in one mouse and establish a new mouse strain from it; this new "transgenic" strain is identical to the original strain except for the one targeted gene modification.[99] Scientists have created hundreds of transgenic mouse strains, each containing a particular modified, added, or deleted gene. These models allow scientists to study the effect of a single gene modification on traits or disorders by comparing the transgenic animals to their unmodified "twin" strain.

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[95] Collins, "Medical and Societal Consequences of the Human Genome Project," 30.

[96] R. Weiss, "For DNA, a Defining Moment," *Washington Post*, May 23, 2000, A01. CFTR stands for cystic fibrosis transmembrane regulator.

[97] See "The Mighty Mouse," in *To Know Ourselves*, U.S. Department of Energy Human Genome Project Information website: *http://www.ornl.gov/hgmis*, visited July 10, 2000.

[98] See S. Blakesee, "Knocking Our Genes Out to Mimic or Cure Disease," in *Blazing a Genetic Trail*, Howard Hughes Medical Institute website: *http://www.hhmi.org/genetictrail*, visited July 10, 2000.

[99] As mice, similar to humans, have two copies of each gene, scientists can alter one or both gene copies. Transgenic mice often contain an additional, inserted copy of a modified gene. See O. Smithies, "Animal Models of Human Genetic Diseases," *Trends in Genetics* 9 (1993): 112. Transgenic mice that have had both functional copies of a particular gene permanently deleted from the genome are called "knockout" mice. See M. R. Capecchi, "Targeted Gene Replacement," *Scientific American* 270 (1994): 52.

For example, scientists created transgenic mice that had a mutation in the gene associated with the human autosomal recessive disorder Huntington disease.[100] Creation of this transgenic mouse, in which the huntingtin gene contains an increased number of CAG repeats,[101] allows scientists to study the molecular and physiological processes of Huntingon disease onset and environmental factors that may influence it. Transgenic mice also allow studies of possible medical interventions.

## *The Human Genome Project*

### *Gene Mapping and Identification*

The Human Genome Project was launched in 1990 as an international, publicly funded research project to determine the DNA sequence of all three billion bases of the human genome and to "map" all the human genes to the twenty-four human chromosomes.[102] In the United States, the major agencies that fund and oversee Human Genome Project research are the National Human Genome Research Institute (NHGRI) and the U.S. Department of Energy (DOE).[103] Initial project goals also included the following: (1) sequencing of other "model organisms," including microbial, roundworm, and fruitfly genomes, to provide comparative information needed to understand how the human genome functions;[104] (2) development of DNA sequencing and analysis technologies to enable completion of project goals; and (3) addressing potential ethical, legal, and social implications of sequencing the human genome.[105]

The main goal of the Human Genome Project was to establish a complete DNA map for all twenty-four human chromosomes by 2005.[106] Project plans were reorganized and accelerated in 1998, in response to an announcement by a private Maryland-based company, Celera Genomics, that it would use a new generation of DNA sequencing technology and a somewhat different technical approach to sequence the human genome

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[100] For a discussion of Huntington disease, see page 16, this chapter. For a discussion of the use of transgenic mice in Huntington disease studies, see N. Wexler, "The Human Genome — Prognostications and Predispositions," in *Annals of the New York Academy of Sciences* 882 (1999): 22, 27–28.

[101] For a discussion of trinucleotide repeat mutations, see page 10, this chapter.

[102] Rowen, Mahairas, and Hood, "Sequencing the Human Genome," 605. For a detailed description of the Human Genome Project's approaches and progress, see the U.S. Department of Energy Human Genome Project Information website: *http://www.ornl.gov/hgmis*, and the National Human Genome Research Institute website: *http://www.nhgri.nih.gov*.

[103] See National Human Genome Research Institute website: *http://www.nhgri.gov*, visited July 7, 2000; U.S. Department of Energy Human Genome Project Information website: *http://www.ornl.gov/hgmis*, visited July 7, 2000. The major international partner is the Sanger Center in Cambridge, England, funded by the Wellcome Trust.

[104] See U.S. Department of Energy, *Understanding Our Genetic Inheritance, The Human Genome Project, The First Five Years: Fiscal Years 1991–1995* (April 1990, NIH Publication No. 90-1050), U.S. Department of Energy Human Genome Project website: *http://www.ornl.gov/hgmis/project/5yrplan/summary.html*, visited July 7, 2000.

[105] Ibid. For further discussion, see Chapter 11, page 318.

[106] U.S. Department of Energy, *Understanding Our Genetic Inheritance, The Human Genome Project, The First Five Years*.

independently.[107] In June 2000, five years ahead of schedule, the international public consortium and Celera Genomics jointly announced that they had completed, or were very close to completing, this goal.[108]

Once the ordering of all three billion letters of the human genome is complete, however, much work still remains. The next major task is annotation of the data, using bioinformatics — the use of computer tools to sift through the mounds of sequence data and identify individual genes that comprise only about 3 percent of the human genome.[109] One commentator reports that new databases and computer programs to annotate the human genome "are cropping up monthly" and will provide the "sextant, compass and charts that will enable researchers to navigate the genome."[110] Most agree that complete annotation is likely to take years.[111]

In addition to using computer programs that scan the genome for recognizable sequences of DNA that are characteristic to the coding sequences of genes, another useful approach in pinpointing human genes and gaining insight into their function is comparative genomics — comparison of the human genome sequence with the genome of other organisms, including mice and other mammals.[112] Both the Human Genome Project public consortium and Celera Genomics have announced their intentions to sequence the three billion bases of the mouse genome.[113] Researchers at Celera Genomics predict that when they "overlay" the human and mouse genomes, they may be able to find many of the 35 percent of human genes missed by other approaches.[114]

Bioinformatics and comparative genomics, along with research of thousands of scientists working to unravel the basic biology of specific physiological processes, will speed the annotation process. NHGRI Director Francis Collins predicts that all genes involved in the 4,000 or so single-gene disorders will be identified within the next three to five years and

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[107] See C. J. Venter et al., "Shotgun Sequencing of the Human Genome," *Science* 280 (1998): 1540; see also E. Pennisi, "Finally, the Book of Life and Instructions for Navigating It," *Science* 288 (2000): 2304.

[108] E. Marshall, "Rival Genome Sequencers Celebrate a Milestone Together," *Science* 288 (2000): 2294; R. Weiss and J. Gillis, "Teams Finish Mapping Human DNA," *Washington Post*, June 26, 2000, A01; Pennisi, "Finally, the Book of Life and Instructions for Navigating It," 2304. The public consortium's "composite" genome data are characterized as a "working draft" that includes about 97 percent of the genome; about 85 percent has been mapped to specific chromosomal regions. Celera Genomics had not released its raw data but claimed it to be "99 percent done." Weiss and Gillis, "Teams Finish Mapping Human DNA."

[109] For a discussion of bioinformatics, see B. Goodman, "Blossoming Bioinformatics — The Princeton Bioinformatics Symposium," *H.M.S. Beagle* website: *http://www.hmsbeagle/74/notes/meeting*, visited March 20, 2000.

[110] Pennisi, "Finally, the Book of Life and Instructions for Navigating It," 2306.

[111] Ibid., 2307; F. S. Collins et al., "New Goals for the Human Genome Project: 1998–2003," *Science* 286 (2000): 682, 687.

[112] See S. J. O'Brien, "The Promise of Comparative Genomics in Mammals," *Science* 286 (2000): 458.

[113] Pennisi, "Finally, the Book of Life and Instructions for Navigating It," 2307.

[114] Ibid. In 2000, Celera Genomics announced it has already finished half the mouse genome sequence and will complete within the year.

that most genes that affect risk for more common complex diseases will be identified within seven years.[115]

### *Gene Variation and Function in Health and Disease*

The initial focus of the Human Genome Project has been on generation of a "reference" or "composite" genome sequence, derived from analysis of anonymous DNA samples provided by a limited number of persons, which highlights the set of human genes that all humans share.[116] The next steps will focus on: (1) DNA sequence variations that exist for specific genes in the human population and may affect disease risks; (2) differences in how those genes are expressed, or "turned on," to produce mRNA and protein in different healthy and diseased tissues; and (3) the structure and function of the protein products of newly discovered genes.

#### *Identification of Gene Variants*

Positional cloning studies can identify human gene variants that cause fully or highly penetrant disorders within families, such as Huntington disease or breast cancer linked to BRCA gene mutations. When a particular gene variant has a more subtle and variable effect on a trait or disorder, as for most common complex disorders, discovering the links between the gene variant and a disorder is much more difficult. The science that studies the association of these genetic variants with disease in population groups is molecular epidemiology.[117] Population-based studies, called association studies, compare the prevalence of particular DNA markers in unrelated individuals affected or unaffected by a particular disorder.[118]

One valuable form of DNA marker is a single-base variant known as a SNP (single nucleotide polymorphism, pronounced "snip").[119] A SNP is a base position in the genome in which two alternative forms occur in the human population at a frequency of greater than 1 percent. SNPs occur about once every 300 to 1,000 bases of the human genome in both coding and noncoding sequence and contribute to variations of traits and disease risk in the human population.[120] In July 2000, a nonprofit consortium of pharmaceutical companies and academic centers[121] and the U.S. Human Genome Project announced that they will work together to identify and place in the public domain

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[115] Ibid.

[116] Ibid., 2305; N. Wade, "Whose Genome Is It Anyway? In a Way, Nobody's," *New York Times*, June 27, 2000, F2. The public consortium project used about ten anonymous donors.

[117] D. Ellsworth, D. M. Hallman, and E. Boerwinkle, "Impact of the Human Genome Project in Epidemiological Research," *Epidemiological Reviews* 19 (1997): 3; see also Chapter 11, page 314.

[118] For a discussion of association studies, see J. A. Todd, "Interpretation of Results from Genetic Studies of Multifactorial Diseases," *The Lancet* suppl. I (1999): 15.

[119] D. G. Wang et al., "Large-Scale Identification, Mapping, and Genotyping of Single-Nucleotide Polymorphisms in the Human Genome," *Science* 280 (1998): 1077.

[120] Collins, "Medical and Societal Consequences of the Human Genome Project," 32; Hagmann, "A Good SNP May Be Hard to Find," 21: Cantor, "How Many SNPs Are Enough?"

[121] The consortium is called the SNP Consortium Ltd., website: *http://snp.cshl.org*, visited February 28, 2000.

125,000 to 250,000 human SNPs.[122] One commentator remarked that this collaborative venture "will speed the development of comprehensive markers that are key to the development of . . . personalized genetic-based medicine."[123]

***Gene Expression Studies***

A complementary approach to understanding gene function and its relation to disease is to sample different human tissues in both healthy and diseased individuals and to compare which genes are "turned on" and "turned off" in healthy and diseased tissues. To do this, researchers produce and compare "complementary" DNA (cDNA) samples from tissue-specific mRNA.[124] By analysis of specific cDNA "expression profiles," from different types of healthy tissues, researchers can determine which genes are important for specific tissues and functions, for example, neuronal functions in the brain.[125] Variations in the types and levels of specific cDNAs in healthy and diseased tissue, for example, in normal versus cancerous breast tissue, can provide information about the roles of particular genes in disease processes.

### *Protein Studies*

Proteins are the specific products encoded by genes that form the body and perform virtually all of its biochemical functions. With completion of the human genome sequence, many in the research community, including Celera Genomics, see a next logical step as proteomics — "an effort to identify all the proteins expressed in an organism and then track their ebb and flow."[126] Researchers also can analyze the protein "profiles" in both healthy and diseased tissues.[127]

Working from genomic and protein profile data, researchers can go a step further and make pure preparations of specific proteins to study their structure and function, referred to by some as "structural genomics"[128] and "functional genomics."[129] Approaches

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[122] K. Pallarito, "Human Genome Project, SNP Consortium Collaborate on New Genetic Markers," *Reuters Health Information*, July 12, 2000, website: *http://www.reutershealth.com*, visited July 12, 2000; see also E. Marshall, "Drug Firms Create Public Database of Genetic Mutations," *Science* 284 (1999): 406.

[123] Pallarito, "Human Genome Project, SNP Consortium Collaborate on New Genetic Markers" (quoting Dr. Paul Billings, cofounder of the San Francisco-based genetic information and consulting firm GeneSage).

[124] See page 7, this chapter. cDNA is a stable copy of mRNA. See Chapter 2, page 37.

[125] Lander, "The New Genomics," 537–538.

[126] R. F. Service, "Can Celera Do It Again?" *Science* 287 (2000): 2136.

[127] K. Fodor, "Celera Shifts to Patentable Discoveries," *Reuters Health Information*, June 28, 2000, website:
*http://www.reutershealth.com/archive*, visited June 28, 2000.

[128] See A. Pollack, "The Next Chapter in the Book of Life Is Written in the Proteins," *New York Times*, July 4, 2000, F1.

[129] P. Heiter and M. Boguski, "Functional Genomics: It's All How You Read It," *Science* 278 (1997): 601; S. Fields, "The Future Is Function," *Nature Genetics* 15 (1997): 325.

include the use of techniques such as X-ray crystallography or nuclear magnetic resonance to study a protein's unique structure.[130] Proteins, with their twenty amino acid alphabet "letters," are structurally more complex than genes, containing numerous loops and folds. These studies can provide important clues about the physiological function of a protein — for example, whether it occurs in a cell membrane, is a secreted molecule, or is likely to bind to DNA, in which case it may have a job in regulating the "turning on" of other genes. Protein structure also can guide researchers in drug design, for example, by knowing what part of a protein to block to prevent its activity.[131] Another approach to studying protein function is to identify the other, sometimes better defined, proteins that bind to and work with the new protein of interest.[132]

**Conclusion and Outlook**

As the follow-up stage of human genome research continues, researchers will not only discover new genes and proteins but also will eventually identify how gene expression is regulated and how different gene and protein expression profiles are linked, in concert with environmental factors, to health and disease. In the more distant future, this will enable scientists to identify the molecular components of disease pathways and to design medical interventions. In the next several years, many predict, it will lead to expanded development of predictive genetic tests and to a form of medical practice tailored to the inherited genetic variations among individuals, the subject of this report.

[130] Pollack, "The Next Chapter in the Book of Life Is Written in the Proteins."
[131] Ibid.
[132] Fields, "The Future Is Function," 325.

# 2

## Introduction to Genetic Testing and Screening

Genetic testing is the use of laboratory procedures to identify specific variations in the form or number of genes or chromosomes in an individual. In this report, we are focusing on tests to detect inherited gene variants present in virtually every cell of an individual, not acquired mutations that happen in single cells during the course of an individual's lifetime.[1] In the clinical setting, genetic testing is used to diagnose or predict particular disorders for individuals and/or their descendants. Currently, clinical genetic testing to diagnose or detect predispositions to over 400 genetic disorders is available.[2]

In the clinical context, the terms genetic testing and genetic screening are sometimes used interchangeably, although they have distinct meanings. The term genetic testing generally refers to testing targeted to an individual based on a perceived risk because of that individual's family and/or medical history. The term genetic screening refers to systematic population-based genetic testing, independent of family history or disease symptoms.[3] Screening can be targeted to an entire population or to specific subpopulations, based on known risks for population groups. An example of population-based screening is screening of newborns for specific inherited disorders, such as phenylketonuria (PKU), which is required by law in all states.[4] In some screening programs, an initial, less precise, test may be used to target a smaller population of potentially at-risk individuals for more precise follow-up genetic testing.

## Uses of Genetic Testing and Screening

Genetic tests are performed for different purposes and at different points in an individual's lifetime. The major categories of genetic testing and screening are outlined in this section.

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[1] For a discussion of acquired mutations and their role in cancer, see Chapter 1, page 11.

[2] GeneTests™, a genetic testing resource funded by the National Library of Medicine of the National Institutes of Health and the Maternal and Child Health Bureau of the Health Resources Services Administration, website: *http://www.genetests.org*, visited May 9, 2000. As of May 2000, laboratories registered with GeneTests™ offered clinical genetic tests, for which testing results are provided to individuals tested, for 419 disorders. Registered laboratories also offer research testing, an earlier stage of test development in which results are not provided to the individual tested, for several hundred additional disorders.

[3] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 4, 65. For a discussion of genetic screening, see Chapter 5.

[4] See page 40, this chapter; for a discussion of newborn screening, see Chapter 6.

## Genetic Testing to Diagnose Disorders

Diagnostic genetic testing may be performed to obtain information about an individual's genetic makeup for the purpose of confirming a diagnosis based on symptoms.[5] Generally, clinicians perform diagnostic genetic testing when a patient shows signs and/or symptoms of a single-gene disorder — one in which inheritance of a single mutated gene variant, or pair of gene variants, leads to disease with virtual certainty.[6] In the clinical setting, examples include DNA-based gene testing to confirm the diagnosis of cystic fibrosis in a young child with recurrent pulmonary infections and testing for X-linked muscular dystrophy (Duchenne/Becker) in a boy who shows characteristic muscle weakness and loss of motor control.[7]

### Predictive Genetic Testing and Screening

Predictive testing is performed on healthy, asymptomatic persons to confirm or exclude a perceived risk for a future genetic condition in the persons themselves or in their descendants. In this report, we consider predictive genetic testing to include newborn screening tests,[8] reproductive testing, and testing of individuals for late-onset disorders.[9] The goal of predictive testing often is to prevent the manifestation of genetically based disorders in individuals and/or their descendants. Intervention to prevent the manifestation of genetic diseases in individuals who have inherited susceptibility mutations[10] is called phenotypic prevention.[11] Genotypic prevention is the prevention of the transmission of disease-associated mutations to new generations.[12]

In addition to disease-associated testing to predict future health risks, genetic testing also includes pharmacogenetic testing to individualize drug treatments to obtain maximal benefit and minimal adverse effect for each patient.[13] Eventually, it also is likely to include genetic testing to determine an individual's risk susceptibility for specific environmental agents, including workplace chemicals.[14]

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[5] This definition will be used throughout this report; the term diagnostic testing also may be used more broadly to include predictive testing of asymptomatic individuals.

[6] For a discussion of single-gene diseases, see Chapter 1, page 14.

[7] Diagnostic testing also may be performed to test for acquired mutations in a cancer biopsy specimen. For example, alterations to a gene called HER-2 are detectable in 30 percent of primary breast cancer biopsies and indicate patients that are likely to respond to a particular chemotherapeutic agent. S. J. Nass, H. A. Hahm, and N. E. Davidson, "Breast Cancer Biology Blooms in the Clinic," *Nature Medicine* 4 (1998): 761.

[8] For a discussion of newborn screening, see Chapter 6.

[9] For a discussion of reproductive and late-onset genetic testing, see Chapter 3.

[10] See Chapter 1, page 18; see also Chapter 3, page 62.

[11] E. T. Juengst, "Caught in the Middle Again: Professional Ethical Considerations in Genetic Testing for Health Risks," *Genetic Testing* 1 (1997/1998): 189, 197.

[12] Ibid.

[13] For a discussion of pharmacogenetics, see Chapter 3, page 74.

[14] For a discussion of biomarkers of susceptibility, see Chapter 3, page 75.

### Genetic Testing for Research

Residual tissue or blood samples obtained for clinical or research purposes may be used for genetics research. For example, researchers may use tissue samples from individuals from families with a history of a genetic disorder in research to identify a gene linked to the disorder.[15] This approach has been used to identify over 100 genes associated with generally rare single-gene disorders such as Huntington disease and cystic fibrosis. As more genes are discovered, research efforts will progressively attempt to link variants of specific genes with increased susceptibility to more complex disorders.[16]

### Identification Testing

Each individual has a unique genome, and genetic analysis of an individual's DNA variations can produce a type of unique identifier. DNA-based identification testing is used for forensic testing (including crime scene investigations), paternity testing, and other attempts to confirm or rule out family relationships among individuals. This form of testing also is called profile analysis.[17]

## Laboratory Methods of Genetic Testing

A genetic test may search for genetic variation directly by analysis of DNA (DNA-based testing) or of chromosomes (cytogenetic testing). This form of testing is called genotypic testing. Phenotypic testing analyzes protein and metabolic products in the body that result from the presence or absence of certain gene variants.

### DNA-Based Testing

DNA-based testing is the most direct method of genetic testing, and it is widely used for medical testing[18] and for identification purposes. The intent of DNA-based testing is to determine which variant forms of a gene (alleles) an individual possesses.[19] DNA-based testing for inherited gene variants can be conducted using any tissue source and at any point in a person's life, from a pre-implantation embryo (in cases where in vitro

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[15] See Chapter 1, page 21.
[16] See Chapter 11, page 314.
[17] For a discussion of DNA technologies used for profile analysis, see page 33, this chapter.
[18] A GeneTests™ survey of United States laboratories that provide clinical genetic testing (conducted June 6, 1998) showed that for fifty genetic disorders for which tests were offered by the largest number of laboratories (nine to eighty-four laboratories), forty-four disorders were most frequently tested for by direct DNA-based testing. (Four were tested for most frequently by FISH [see page 39, this chapter] and two by indirect linkage analysis [see page 36, this chapter].) Summary report on genetic testing from the GeneTests™ (formerly Helix) Database, in rank order by the number of labs testing for the disease.
[19] See Chapter 1, page 11.

fertilization technologies[20] are used) until, and even after, death.[21] DNA-based testing may scan all or part of a gene associated with a disorder to search for any possible mutation that might impair gene function. Alternatively, it may focus on particular gene variants known to be associated with susceptibility to disease.[22] For example, inheritance of one of three variants of the apolipoprotein E (APOE) gene is associated with increased risk of Alzheimer disease in some populations.[23]

### *DNA Analysis*

*Southern and RFLP Analysis*

In Southern analysis, investigators can process and analyze different genomic DNA samples to look for particular gene variants. A diagram of the process is shown in Figure 4.[24] The starting material is genomic DNA, obtained from a tissue sample such as blood or cheek cell scrapings. The sample contains long strands of DNA molecules that are cut using enzymes that act at specific DNA base sequences ("spellings"). Cutting generates millions of DNA fragments that are several hundred to tens of thousands of base pairs long.[25] Investigators place the fragmented DNA samples from one or more individuals at different positions along the top of rectangular gel, along with control samples.[26] An electric current is applied along the length of the gel, separating the DNA fragments of each sample according to size. The separated DNA samples in the gel then are transferred to a filter paper.

The next step is based on a fundamental process used in many DNA-based testing techniques, called nucleic acid hybridization. Hybridization occurs when two single-stranded DNA molecules combine and form a double-stranded molecule.[27] Molecules combine based on the principle of "base pair complementarity," by which each of the four chemical bases of DNA bind to a specific counterpart — A to T and C to G.[28] Using

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[20] In vitro fertilization technologies use laboratory techniques to mix egg and sperm cells in laboratory dishes and generate embryos that are later implanted into the prospective mother's uterus. See New York State Task Force on Life and the Law, *Assisted Reproductive Technologies — Analysis and Recommendations for Public Policy* (New York State Task Force on Life and the Law: New York, April, 1998). See also Chapter 3, page 53.

[21] Testing can be performed using stored tissue samples years after a person's death.

[22] For a discussion of allele variation, see Chapter 1, page 11.

[23] See Chapter 1, page 18; for a discussion of genetic risk for Alzheimer disease, see Chapter 3, page 67.

[24] See Appendix B, page 406.

[25] DNA-cutting enzymes, called restriction enzymes, cut at "motifs" of four, six, or eight base pairs, generating average sized fragments of <300, 4,000, and 64,000 base pairs, respectively. There are hundreds of different restriction enzymes, each cutting at a specific motif. For more information about DNA restriction and cloning, see the U.S. Department of Energy Human Genome Project Information website: *http://www.ornl.gov/ngmis/faq/faqs1.html*, visited April 7, 1998.

[26] For any test, prior research determines which cutting enzyme to use and what variants to look for. Controls are reference samples of normal and identified mutant variants to which test samples are compared.

[27] Hybridization also can occur between a single-stranded DNA molecule and an RNA molecule. See page 37, this chapter.

[28] See Chapter 1, page 6.

this principle, investigators design "probes," single-stranded DNA molecules containing a specific base sequence that will bind only with matching single-stranded genomic DNA on the filter.[29] For example, a DNA strand with the sequence A-T-G-A-T-A-G-G-C-T-T-A-G-T-T-G-C-A will bind specifically to its complementary sequence, T-A-C-T-A-T-C-C-G-A-A-T-C-A-A-C-G-T.

The probe is tagged with radioactive marker[30] and added to a fluid that bathes the filter, allowing it to hybridize specifically to complementary DNA in samples on the filter. The investigator then rinses the filter and places a piece of X-ray film on top of the filter. Hybridized fragments in each sample show up as dark bands on a light background of the film. For example, if the particular DNA fragment of interest in one sample has undergone a large DNA deletion mutation inside the cutting sites,[31] the size difference between that fragment and the larger normal-sized fragment of another sample would affect their movement through the gel — the smaller fragment would migrate faster. Differences would be detectable on the X-ray film.

Southern analysis can detect variants in genomic DNA of even a single base because mutation of a single base can change the susceptibility of a DNA segment to DNA-cutting enzymes.[32] For example, an enzyme called HindIII recognizes and cuts the sequence motif AAGCTT. If a single base is changed — for example, the G is changed to A, generating the new sequence motif AAACTT — the site will not be cut. As a result, cutting occurs at different sites for the different variants, generating different size fragments on the filter. This approach has been used to distinguish normal and sickle cell beta globin gene variants, which vary by a single base.[33]

The use of Southern analysis specifically to determine genomic variation among individuals is called RFLP (restriction fragment length polymorphism) analysis. RFLP analysis is used for individual identification, or profile analysis. Profile analysis focuses on DNA sequences at particular genomic "landmarks" that show common variant forms within a population. The landmarks examined do not provide medical information and generally are repetitive stretches of noncoding DNA.[34] These repetitive segments are composed of a short "core" sequence that is repeated many times. All individuals share a particular landmark, but they show variability in the number of repeats and the overall size of the landmark. These size differences can be detected by Southern RFLP

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[29] The probe may consist of any genomic fragment (coding or noncoding DNA) that has been cloned to generate many copies. For Southern analysis, probes are generally hundreds of bases long, and their ability to bind to DNA on the filter does not require 100 percent complementarity. For very short DNA probes of fifteen to twenty bases, 100 percent complementarity is needed. For discussion, see R. W. Thompson, R. R. McInnes, and H. F. Willard, *Genetics in Medicine*, 5th ed. (Philadelphia: W. B. Saunders Company, 1991), 104–108.

[30] Fluorescent labels also may be used.

[31] A deletion or insertion mutation of 100 bases or more would be detectable.

[32] Mutation also can create newly susceptible sites for cutting that are not present in the original sequence.

[33] Thompson, McInnes, and Willard, *Genetics in Medicine*, 253; J. C. Chang and Y. W. Kan, "A Sensitive New Prenatal Test for Sickle Cell Anemia," *New England Journal of Medicine* 307 (1982): 30.

[34] See Chapter 1, page 9.

analysis.[35] RFLP analysis of multiple landmarks generates a complex pattern, called a "genetic fingerprint,"[36] which may be sufficient to rule out or confirm identity, for example, of a criminal suspect.[37]

*PCR Analysis*

Polymerase chain reaction (PCR), developed in the mid-1980s, has greatly expanded the range of DNA-based testing. PCR copies, or "amplifies," targeted segments of genomic DNA up to a billion-fold, within a few hours.[38] It can be performed using minute samples, even a single cell. As a result, PCR is used widely for medical genetic testing and forensic identification purposes.

To perform PCR, investigators place each genomic DNA sample in an individual test tube and heat the samples to generate the single-stranded form of DNA. To each sample, they add a DNA-copying enzyme, nucleotide building blocks (A, C, G, and T) with which to make the copies, and pairs of short DNA segments called "primers." Primers, similar to probes, are short DNA strands that bind to specific segments of the genomic DNA sample based on base pair complementarity. Primers act as sequence-specific flags for specific DNA spellings, and they direct the DNA-copying enzyme to copy the adjacent stretch of DNA only.[39]

The copying process extends several hundred bases, converting the single-stranded DNA fragment to double-stranded DNA. Then, investigators heat the test tubes to break the newly formed base pair bonds between the original and the copied DNA strands. When the temperature is again lowered, both strands bind more primer and reinitiate the copying process. This process is continued for twenty to thirty cycles, exponentially increasing the number of copies of the targeted DNA sequence of interest.

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[35] T. D. Gelehrter, F. S. Collins, and D. Ginsburg, *Principles of Medical Genetics*, 2d ed. (Baltimore, MD: Williams and Wilkins, 1998), 80–82; see also page 33, this chapter.

[36] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 81.

[37] In 1997, the U.S. Federal Bureau of Investigation announced that when probability estimations of random matches between individuals are calculated to be less than one in 260 billion, they could be used to confirm identity. C. Holden, "DNA Fingerprinting Comes of Age," *Science* 278 (1997): 1407. Investigators also may use different sets of shorter genomic landmarks that are suitable for PCR. See R. S. Murch and B. Budowle, "Are Developments in Forensic Applications of DNA Technology Consistent with Privacy Protections?" in *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*, ed. M. A. Rothstein (New Haven, CT: Yale University Press, 1997), 216–217; see also N. Wade, "F.B.I. Set to Open Its Database for Fighting Crime," *New York Times*, October 12, 1998, A1, A15.

[38] Prior to PCR, copying of a particular DNA segment required DNA cloning, which could take weeks to months.

[39] The primers are approximately twenty bases long. Two different sequence primers (millions of copies of each) are added to each test tube; they bind to single-stranded complementary DNA on either side of the segment to be copied. See Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 73–74.

PCR-amplified DNA can be analyzed by Southern analysis, as described above, or by a number of other approaches, including DNA sequence analysis.[40] In a technique called allele-specific oligonucleotide hybridization, investigators distinguish gene variants by their differential binding to perfectly complementary short DNA probes (oligonucleotides).[41] This approach also is used to distinguish normal and sickle cell beta globin gene variants. The normal and sickle cell variants can be distinguished using duplicate filters, each bathed with one of two probes that differ by only a single base. One probe would bind to the sickle cell allele only, and the other would bind to the normal allele only.

In recent years, researchers have developed more sophisticated PCR applications that allow highly accurate detection of DNA base variations and high sample "throughput"[42] — the number of tests that can be performed simultaneously.[43]

*DNA Sequence Analysis*

DNA sequence analysis determines the specific sequence of the A, C, G, and T bases of DNA molecules. It is the "gold standard" for detecting mutations.[44] The starting material for DNA sequencing is a pure batch of a particular single-stranded DNA fragment mixed with a pool of nucleotide building blocks (A, C, G, and T) and an enzyme. The enzyme adds the nucleotide building blocks by base pairing to the single strand, one-by-one, generating a new sequence-specific double strand. A typical reaction mix contains many copies of the same growing DNA sequence, at different length extensions. In the course of this reaction, the mixture is "pulsed" with a new ATCG mix in which each of the four nucleotides is tagged with a different color fluorescent dye: red, yellow, green, or blue. The tagged nucleotide building blocks are called "terminator" nucleotides — they are chemically modified in a way that prevents other bases from being added on.

Investigators then analyze the terminated reaction mix to determine the color tag, and the identity of the last nucleotide (A, C, G, or T), of the DNA strands of varying sizes. The tagged DNA mixture is loaded onto a sequencing machine that separates the strands by size and reads the last base of each strand, based on the color of its tag. For example, for a hypothetical DNA sequence, all strands that are 150 bases long end in A, whereas those that are 151, 152, and 153 bases long end in G, A, and C, respectively.

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[40] For discussion of other techniques, see ibid., 87–88; see also G. B. van Ommen, F. Bakker, and J. T. den Dunnen, "The Human Genome Project and the Future of Diagnostics," *The Lancet* 354 suppl. I (1999): 5, 7–8.

[41] These probes are generally fifteen to twenty bases long and are called allele-specific oligonucleotides. See Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 84.

[42] L. M. Fisher, "Biology Meets Technology — Biochips Signal a Critical Shift for Research and Medicine," *New York Times*, December 21, 1999, C1.

[43] M. M. Shi, M. B. Bleavins, and F. A. de la Iglesia, "Technologies for Detecting Genetic Polymorphisms in Pharmacogenomics," *Molecular Diagnosis* 4 (1999): 343, 346–348.

[44] Ibid., 348.

This information enables investigators to spell out the whole base sequence of a DNA strand.[45]

Some clinical genetic tests sequence all or part of the gene of interest. For example, a commercially available test to detect mutations in a gene called BRCA1[46] that are associated with increased risk of breast and ovarian cancer scans the whole gene coding sequence, approximately 7,800 bases, to search for hundreds of different mutations.[47] However, once a specific mutation is identified within a family, the testing of additional family members can be simplified to determine the presence or absence of that specific mutation.

Sequencing technology has evolved over the course of the ten-year Human Genome Project, from about $10 per DNA unit to about 4 cents a unit.[48] In one key advance, in 1998, commercial researchers developed a new generation of a more rapid DNA sequencing technology called capillary sequencing, which performs with significantly higher speed, sensitivity, accuracy, and resolution at lower cost and minimal hands-on operator time.[49] These technological developments enabled researchers to complete the sequencing of the human genome by June 2000, years ahead of the goal.[50]

*Linkage Analysis*

Linkage analysis is an indirect method of DNA-based genetic testing. It traces inheritance of highly penetrant disease-associated genes that have not yet been identified but that have been located (mapped) to a specific region of a specific chromosome.[51] Investigators use catalogued genomic DNA markers located on specific chromosomal regions as proxy markers for the unidentified gene.[52] These markers exist in everyone but

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[45] N. Wade, "The Struggle to Decipher Human Genes," *New York Times*, March 10, 1998, F1; E. Pennisi, "The Human Genome Project: The Key to Success Is Finishing Well," *Science* 280 (1998): 816. For step-by-step graphic presentation of this process, see Celera Genomics Corporation Genomics Education Module, Celera Genomics Corporation website: *http://www.celera.com*, visited July 21, 2000.

[46] The BRCA1 gene, when mutated, can increase risk for breast and/or ovarian cancer. See Chapter 3, page 63.

[47] Program materials, Myriad Genetics; A. Abbott, "Complexity Limits the Power of Prediction," *Nature* 379 (1996): 390.

[48] N. Wade, "Double Landmarks for Watson: Helix and Genome," *New York Times*, June 27, 2000, F5.

[49] See J. G. Venter et al., "Shotgun Sequencing of the Human Genome," *Science* 280 (1998): 1540; J. C. Mullikin and A. A. McMurray, "Sequencing the Genome, Fast," *Science* 283 (1999): 1867; see also Y. Baba, "Capillary Gel Electrophoresis: New Technique for Specific Recognition of DNA Sequence and the Mutation Detection on DNA," *Journal of Biochemical and Biophysical Methods* 41 (1999): 91, 92.

[50] See Venter et al., "Shotgun Sequencing of the Human Genome," 1540; see also Wade, "Double Landmarks for Watson: Helix and Genome," F5.

[51] For a discussion of gene penetrance, see Chapter 1, page 13; for a discussion of gene mapping, see Chapter 1, page 23.

[52] For discussion of DNA markers, see Chapter 1, page 25. The markers used in linkage analysis must be present in all individuals but show some variation (polymorphism) among different individuals, so that

show variations among individuals, enabling investigators to trace the variant forms of the marker within families. Individuals with the disease-associated allele would likely share the same marker variant, and those without that allele would lack it. The linkage test would be performed to determine which additional family members have inherited the marker variant and, by inference, the closely linked disease allele. Linkage analysis is highly, but not 100 percent, accurate.[53]

Once researchers identify a gene and determine its DNA base pair sequence, direct testing replaces indirect linkage analysis. For example, direct DNA-based testing has replaced linkage analysis for cystic fibrosis and Huntington disease testing.

### *RNA Analysis*

Mutations in a gene's coding sequence are copied into the complementary mRNA intermediates that the cell uses to make protein.[54] For certain types of mutations (e.g., deletion of all or part of the gene), mRNA may not be produced at all, or the number of mRNA copies produced by the gene may vary. In some cases, investigators may wish to examine mRNA instead of DNA. They can do so using DNA-based testing methods, with some adaptations.

#### *Northern Analysis*

One technique to analyze mRNA, called Northern analysis, is conceptually related to Southern analysis. mRNA samples are size-separated in a gel by electric current, blotted to a filter, and then bathed in a fluid containing tagged DNA probes. Single-stranded DNA probes bind to complementary mRNA molecules on the filter. Northern analysis can detect some of the base sequence differences between samples as Southern analysis of DNA. It also can show changes in the quantity of mRNA molecules produced by gene variants. If a mutation alters the number of mRNA molecules copied from a gene, the number of tagged probe molecules that bind the filter will change proportionally, and the fluorescent or radioactive signal produced by the bound probe can be quantitated.

#### *Protein Truncation Testing*

mRNA also can be used for other DNA-based testing methods if it is first "copied" from RNA to its more stable DNA form, called complementary DNA (cDNA).[55] This approach is used in protein truncation testing, which detects particular types of mutations called nonsense mutations; these mutations cause production of incomplete

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maternal versus paternal chromosome segments can be traced. Linkage analysis is one of the steps in positional cloning. See Chapter 1, page 21.

[53] During meiosis (the series of cell divisions that generate egg and sperm cells), even closely linked chromosomal segments can be separated by chromosomal recombination. See Chapter 1, page 8.

[54] For discussion of mRNA, see Chapter 1, page 6.

[55] See Chapter 1, page 26.

(truncated) proteins.[56] Nonsense mutations are common for particular gene disorders. For example, they account for about 80 percent of heritable clinically relevant mutations in a gene called APC (adenomatous polyposis coli), resulting in a form of familial colon cancer.[57]

For protein truncation testing, investigators start with an mRNA sample and convert it to its cDNA form.[58] They then use PCR to generate many copies of the particular cDNA molecule that corresponds to the gene of interest (for example, the APC gene). Next, they use the purified PCR sample to make protein in a test tube and analyze the size and quantity of the protein produced.[59] For some genes, such as APC, protein truncation testing may provide a fast and convenient alternative to other DNA-based testing methods.[60]

### Cytogenetic Testing

#### *Karyotype Analysis*

In 1956, researchers developed a technique to analyze the structure and number of chromosomes in an individual's genome. This technique, called karyotype analysis,[61] requires a small blood or tissue sample.[62] Investigators treat the sample to stimulate cell division and then "arrest" dividing cells at a particular stage in which chromosomes are tightly condensed. They then "stain" condensed chromosomes, generating chromosome-specific banding patterns. From photomicrographs of these stained chromosomes, investigators arrange the chromosome content of a single cell, showing aligned chromosome pairs that are discernible by size, structure, and banding patterns. This arrangement, called a karyotype, is reported by first listing the number of chromosomes per genome, followed by the sex chromosome content, followed by any abnormalities in chromosome number or structure. A normal male karyotype is 46, XY. A karyotype for a male with Down syndrome (caused by inheritance of an extra copy of chromosome 21) is 47, XY, +21.[63]

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[56] See Chapter 1, page 10. The end product of protein truncation testing is a particular protein. Due to the use of mRNA samples as starting material, the method is classified here as an RNA test rather than as a protein test.

[57] R. van der Luijt et al., "Rapid Detection of Translation-Terminating Mutations at the Adenomatous Polyposis Coli (APC) Gene by Direct Protein Truncation Test," *Genomics* 20 (1994): 1; G. M. Petersen et al., "Genetic Testing and Counseling for Hereditary Forms of Colorectal Cancer," *Cancer* 86 suppl. (1999): 1720, 1722. For a discussion, see page 44, this chapter, and Chapter 8, page 222.

[58] See page 37, this chapter.

[59] These cDNA-derived samples, unlike genomic DNA, contain only coding (exon) sequences and no noncoding (intron) sequences, allowing them to be directly translated into protein. See Chapter 1, page 9.

[60] van der Luijt et al., "Translation-Terminating Mutations," 1; see also Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 270.

[61] Thompson, McInnes, and Willard, *Genetics in Medicine*, 13.

[62] Samples include fetal or chorionic cell samples obtained by amniocentesis or chorionic villus sampling. See Chapter 3, page 51.

[63] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 153–158.

### *Fluorescence in Situ Hybridization Analysis (FISH)*

Major advances in cytogenetics now enable investigators to analyze precisely molecular variations of particular chromosomes. The chief approach is called FISH (fluorescence in situ hybridization analysis).[64] FISH combines the approaches of karyotype analysis and DNA probe hybridization. Chromosomal samples are prepared and bathed with fluorescence-tagged DNA probes to one or more gene variants of interest. The samples are then examined microscopically. Chromosomes containing the DNA variant of interest show a detectable fluorescent patch. Investigators also may use mixtures of probes that bind to many sites on a particular chromosome; this is called "chromosome painting." For example, chromosome 21 painting to test fetal cells for Down syndrome uses a mixture of probes that cover that chromosome to determine whether individual cells contained three versus two painted chromosomes. FISH also can analyze multiple genes and chromosomes simultaneously. By combining five primary fluorescent dyes in different ratios and using sophisticated imaging techniques, investigators can paint and analyze the twenty-four human chromosomes of a sample.[65] FISH can be performed using only a single cell.

## Gene Product and Metabolite Analysis

Each of the many thousands of proteins in the human body is the "product" of a specific gene. Among individuals, variation in structural and/or functional properties of a particular protein reflects variation in the coding gene.[66] Tests that can precisely identify these protein variations are considered a type of genetic testing. When the protein product is an enzyme, the activity or activity-related substances of that enzyme also may be tested by metabolite analysis.

### *Protein Analysis*

#### *Electrophoresis*

Electrophoresis distinguishes protein variants based on differences in electrical charges, which result from changes in a protein's building blocks, amino acids. Electrophoresis subjects protein samples to an electric current. Proteins with different overall electrical charges will migrate at different rates. This approach has been used for decades to distinguish normal from sickle cell beta hemoglobin proteins in blood samples. Sickle cell and normal beta hemoglobin proteins migrate at different rates, due

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[64] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 158–162.
[65] Ibid., 159.
[66] See Chapter 1, page 10.

to a single amino acid change.[67] This method has the advantages of simplicity, low cost, standardization, and reliability.[68]

*Antibody-Based Protein Analysis*

Antibodies are proteins of the immune system that recognize and bind to other proteins with exquisite specificity. Investigators can produce antibodies that recognize specific proteins and, in some cases, different variants of a particular protein. One type of antibody-based test, called Western analysis, is conceptually related to Southern and Northern analysis. It uses an electric current to separate protein molecules in a gel based on protein mass. Similar to Southern and Northern analysis, the separated molecules in the gel are then transferred to a filter that is bathed in a fluid containing tagged markers. In Western analysis, the tagged markers are not DNA probes; they are labeled antibodies. Western analysis can detect differences in size and amount of specific proteins in different samples. For example, Western analysis has been used to determine the presence, absence, or alteration of the muscle protein dystrophin. This protein is absent in X-linked Duchenne muscular dystrophy, and the size of the protein is altered in X-linked Becker muscular dystrophy.[69]

***Metabolite Analysis***

For single-gene disorders in which the affected protein is an enzyme, it is possible to test for changes in the enzyme's activity or for changes in levels of the enzyme's metabolites (the substrate that it acts upon or the product it produces). One example is carrier testing for Tay-Sachs disease.[70] This universally lethal disease results from a deficiency in an enzyme called hexosaminidase A. Carriers have half the normal level of enzyme. The test quantitates enzyme levels by measuring the ability of a blood sample to convert an artificial substrate to a product. This conversion generates a colored product, which can be quantitated.[71]

Another metabolite test detects individuals affected by the autosomal recessive disorder PKU, which causes progressive mental retardation. PKU results from a deficiency of the enzyme phenylalanine hydroxylase. Unlike the Tay-Sachs test, which measures enzyme activity, the PKU test measures blood levels of the enzyme's substrate, the amino acid phenylalanine. Elevated blood levels indicate that the enzyme required to convert phenylalanine to another amino acid called tyrosine may be defective or missing.[72]

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[67] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 100. In sickle cell beta globin protein, the electrically neutral amino acid valine is replaced by the negatively charged amino acid glutamic acid.

[68] National Institutes of Health Consensus Conference, "Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies," *Journal of the American Medical Association* 258 (1987): 1205, 1206.

[69] Thompson, McInnes, and Willard, *Genetics in Medicine*, 113.

[70] For discussion of carrier testing, see Chapter 3, page 50.

[71] M. Kabach et al., "Tay-Sachs Disease — Carrier Screening, Prenatal Diagnosis, and the Molecular Era," *Journal of the American Medical Association* 270 (1993): 2307.

[72] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 293.

## Limitations and Complexity of Genetic Testing

### Limits to Analytical Validity

The analytical validity of a genetic test is a measure of how well it is designed and performed in the laboratory to detect what it is supposed to detect. It encompasses two factors — the test's sensitivity and its specificity. The analytical sensitivity of a genetic test is the probability that the specific DNA, mRNA, or protein variant being searched for in the sample will be detected when present. The analytical specificity of a genetic test is the probability that the test will be negative when the variant DNA, mRNA, or protein tested for is absent from the sample.[73]

*Limits to Clinical Validity*

Clinical validity measures the extent to which an analytically valid test result can diagnose or predict a particular disease or disorder. It includes several components: (1) clinical sensitivity, the probability that the test will be positive in someone who will manifest the disease; (2) clinical specificity, the probability that a test will be negative in someone who will remain free of disease; (3) positive predictive value, the probability that someone with a positive test result will get the disease; and (4) negative predictive value, the probability that someone with a negative test result will not get the disease.[74] For DNA-based genetic tests, there are several factors that may limit clinical validity.

***Limits to Clinical Sensitivity*: *Genetic Heterogeneity***

Similar or identical disorders may be caused by different mutations of a single gene (allelic heterogeneity) or different genes (locus heterogeneity).[75] Most DNA-based tests cannot detect all potential mutations that might affect risk for a particular disease. This fact decreases a test's clinical sensitivity and produces clinical "false negative" test results.

Most genetic disorders, including single-gene disorders, show allelic heterogeneity. Exceptions, such as sickle cell disease, which is associated with a single point mutation, are rare.[76] Generally, the larger a gene is, the greater the number of allelic variants. For example, three large genes, BRCA1 (breast cancer susceptibility 1), BRCA2

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[73] For metabolite testing, sensitivity and specificity are determined by a quantitative test using a predetermined cutoff level. National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing,* ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of Health, 1997), 25, 179–180.

[74] These four parameters are interrelated and can be calculated by correlating data on disease incidence and genetic test results within a specific population group. See NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 24–28.

[75] See Chapter 1, page 14.

[76] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 29.

(breast cancer susceptibility 2), and CFTR (cystic fibrosis transmembrane regulator) genes, each have over 100 identified clinically relevant mutations.[77] As a further complication, different variants exist within different racial or ethnic subpopulations. For example, one mutation accounts for approximately 70 percent of all cystic fibrosis mutations in Caucasian Americans, but only 48 percent in African Americans and 30 percent in Asian Americans.[78]

Different DNA-based genetic test methods have different limits to their sensitivity. For example, protein truncation testing will not detect missense mutations that change amino acid composition but do not stop protein production. Even DNA sequence analysis of an entire gene coding sequence is not 100 percent sensitive. Mutations that occur outside the coding region of a gene, sometimes thousands of bases away, can impair normal expression ("turning on") of the gene. For some disorders, such as the blood disorder hemophilia A, these types of mutations are common.[79]

Locus heterogeneity also can limit sensitivity. A negative test result for one identified gene does not rule out an inherited mutation at another, perhaps unidentified, gene. For example, mutations of one of two identified genes, BRCA1 and BRCA2, confer an increased risk for breast and ovarian cancer, but they account for only 80 percent of all families that show a single-gene pattern of breast cancer susceptibility.[80]

### *Limits to Predictive Value*

For single-gene disorders such as Huntington disease and Tay-Sachs disease, a positive test result provides 100 percent predictive value. However, susceptibility mutations for more complex disorders show incomplete penetrance; inheritance of a susceptibility mutation is not associated with disease 100 percent of the time.[81] Even for a specific mutation, the incidence of the associated disease may vary among families or population groups. For example, data show that while BRCA1 and BRCA2 gene mutations confer an 85 percent risk for breast cancer within some families, these mutations may pose a significantly lower risk to individuals outside those high-incidence families.[82]

Variable range and severity of symptoms and age of onset also complicate the interpretation of DNA-based tests.[83] For some disorders, a positive test result may be

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[77] F. S. Collins, "Lots of Mutations, Lots of Dilemmas," *New England Journal of Medicine* 334 (1996): 186; National Institutes of Health, *Genetic Testing for Cystic Fibrosis*, NIH Consensus Statement 15 (Bethesda: National Institutes of Health, 1997), 7, 8.

[78] National Institutes of Health, *Genetic Testing for Cystic Fibrosis*, 7, 8.

[79] N. E. Morton, "Genetic Epidemiology," *Annual Review of Genetics* 61 (1993): 523, 525. See also Chapter 3, page 64.

[80] A. Abbott, "Complexity Limits the Power of Prediction," *Nature* 379 (1996): 390.

[81] For discussion of incomplete penetrance, see Chapter 1, page 13.

[82] B. Healy, "BRCA Genes — Bookmaking, Fortune-Telling, and Medical Care," *New England Journal of Medicine* 336 (1997): 1448; see also Chapter 3, page 65.

[83] See Chapter 1, page 14.

highly predictive for disease incidence but poorly predictive for how an individual will experience a variable range of severity and symptoms. For example, the autosomal recessive disease cystic fibrosis is caused by inheritance of two mutant copies of a gene called CFTR.[84] The large CFTR gene has over 800 identified clinically significant mutations; these mutations are associated, in some cases, with different types of symptoms.[85]

Together, incomplete penetrance, variable expressivity, and variable age of onset lead to problems of prognosis for some single-gene disorder testing. The complexity is magnified when testing for genes involved in more complex diseases, such as heart disease and cancer, which result from an interplay of multiple genes and environmental factors.

Beyond these statistical uncertainties, the rapid translation of genomic research to clinical genetic testing may raise more fundamental scientific uncertainties. In some cases, it may be difficult for scientists to predict whether and how particular gene mutations will affect an individual's disease risks. In some, but not all, cases, scientists may know enough about a protein's structure and function to predict the risks linked to a particular mutation. For example, some who undergo BRCA gene testing learn that they have inherited a BRCA gene variant of "undetermined clinical significance."[86] When the mutation-associated disease risk is uncertain, years of clinical follow-up and data assessment are needed to establish accurate risk information.

### Limits to Clinical Utility

Another important consideration is the clinical utility of a predictive genetic test result. For reproductive testing, preventive options include altered reproductive planning, medical intervention, or pregnancy termination. Predictive genetic tests for late-onset disorders have clinical utility if they enable those testing positive to implement a preventive option, such as drug treatment or early monitoring for signs of disease onset. However, predictive genetic tests may provide risk information in the absence of available clinical interventions, a situation referred to as the "therapeutic gap."[87]

### Genotypic versus Phenotypic Testing for Inherited Mutations

DNA-based testing precisely identifies specific mutations. It can detect variants in any gene and can be done at any point in an individual's lifetime. It can predict phenotypic consequences well in advance, but it is subject to limits in sensitivity and

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[84] For a discussion, see Chapter 5, page 119.

[85] See T. Brown and E. Langfelder Schwind, "Update and Review: Cystic Fibrosis," *Journal of Genetic Counseling* 8 (1999): 137, 147; P. T. Rowley, S. Loader, and J. C. Levenkron, "Cystic Fibrosis Carrier Population Screening: A Review," *Genetic Testing* 1 (1997): 53.

[86] T. S. Frank, "Laboratory Determination of Hereditary Susceptibility to Breast and Ovarian Cancer," *Archives of Pathology and Laboratory Medicine* 123 (1999): 1023. See also Chapter 3, page 64.

[87] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 3.

predictive value, as discussed above. Phenotypic testing of proteins and metabolites, on the other hand, often has a more limited timeframe in which testing can be performed.

Some inherited susceptibility mutations may be tested for by either genotypic or phenotypic tests. Depending on the type and purpose of testing,[88] genotypic or phenotypic testing may present different advantages or disadvantages. For some autosomal recessive disorders, such as cystic fibrosis, phenotypic testing is useful only for diagnosis of persons who have inherited two mutant copies of the CFTR gene. These persons, but not carriers of a single mutant CFTR gene, can be tested using a "sweat" test that detects abnormal levels of chloride in sweat secretions.[89] Carrier testing to detect healthy carriers of one mutant gene variant requires DNA-based testing.[90] Practical issues such as cost and ease of testing, as well as other risks and benefits to individuals,[91] also may require consideration. For some conditions such as PKU, metabolite testing may be used as a first stage-screening test, followed by a more specific (and costly) DNA-based test.[92]

For some genetic conditions, phenotypic testing may be more burdensome. For example, offspring of individuals with familial adenomatous polyposis (FAP), a rare disorder associated with early-onset colon cancer, are at risk for inheriting this fully penetrant, dominant mutation of the APC gene.[93] Before a gene test was available, all offspring from age 10 or 11 would be monitored by colonoscopic examination, an invasive procedure to detect precancerous polyps that are characteristic of the disorder. Now, if a mutation has been identified in affected family members, children can undergo DNA-based genetic testing to determine whether they have inherited the familial mutation. This allows children who test negative to bypass colonoscopic monitoring.[94]

For other conditions, a phenotypic test may be more appropriate than a genotypic test. One example is hereditary hemochromatosis, a late-onset autosomal recessive disease resulting in excessive iron absorption, and ultimately in cirrhosis, diabetes, and cardiac impairment.[95] The gene and the specific mutations associated with this disorder were identified in 1996, and DNA-based testing is available.[96] However, because of uncertainties about the predictive powers of the gene-based test, and considering potential

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[88] See pages 30–38, this chapter.
[89] See Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 221.
[90] See ibid., 222.
[91] See Chapter 3.
[92] Kenneth Pass, Ph.D., Director of Newborn Screening Program, New York State Department of Health, presentation to the New York State Task Force on Life and the Law, January 14, 1998.
[93] See page 38, this chapter.
[94] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 265; R. Weiss, "Genetic Testing Is Not as Simple as It Sounds," *Washington Post*, February 10, 1998, Z06.
[95] For a discussion, see Chapter 5, page 124.
[96] W. Burke et al., "Consensus Statement: Hereditary Hemochromatosis: Gene Discovery and Its Implications for Population-Based Screening," *Journal of the American Medical Association* 280 (1998): 172.

social risks to those who test positive, a 1998 consensus panel recommended that phenotypic serum iron testing may be more appropriate in some circumstances. [97]

## Future Directions in Genetic Testing Technologies

Current DNA-based technologies, combined with the growing human genome database, have revolutionized genetic testing. The currently technologies used clinically, however, are still limited; they focus on one gene and one mutation at a time. Emerging technology is greatly broadening this range, enabling simultaneous analysis of multiple genes and alleles. These new technologies, combined with continued analysis of human gene variations and their association with increasingly complex diseases, will continue to change clinical genetic practice.[98]

### Chip Technology and Microarrays

> *Gene chips will offer a road map for prevention of illness throughout a lifetime*.[99]

One important new technology is the DNA chip, which allows thousands of different DNA segments to be tested simultaneously. DNA chip technology, similar to many other DNA-based methods, is based on hybridization of complementary molecules.[100] A DNA chip is a small glass wafer, about the size of a postage stamp, containing up to several hundred thousand testing spots.[101] Each testing spot contains many copies of a unique, laboratory-synthesized DNA strand about twenty bases long. Chips are designed so that each testing spot contains a different small segment of a gene, and the chip contains all known variations of each gene segment. These comprehensive collections of gene sequences on individual chips are called microarrays. A single microarray can test all possible sequence variants of one or more genes of interest.

How does the test work? A single-stranded genomic DNA sample of the individual to be tested is cut into fragments, and each fragment is labeled with a fluorescent marker. Thus, an entire genomic sample is used as a probe.[102] This labeled sample DNA is then washed over the thousands of different testing spots on the chip. When a segment of labeled genomic DNA encounters a perfectly matched (complementary) DNA strand on a particular testing spot, it binds. For any individual sample, a unique pattern of bound and unbound testing spots will result. After binding, investigators use an optical scanning

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[97] Ibid.

[98] See van Ommen, Bakker, and den Dunnen, "The Human Genome Project and the Future of Diagnostics"; F. S. Collins, "Shattuck Lecture — Medical and Societal Consequences of the Human Genome Project," *New England Journal of Medicine* 341 (1999): 28; D. G. B. Leonard, "The Future of Molecular Testing," *Clinical Chemistry* 45 (1999): 5.

[99] President Bill Clinton, State of the Union Speech, January 27, 1998, quoted in "Getting Hip to the Chip," *Nature Genetics* 18 (1998): 195, 197.

[100] See page 32, this chapter.

[101] R. F. Service, "Microchip Arrays Put DNA on the Spot," *Science* 282 (1998): 396; D. Brown, "DNA-Encoded Chips Appear to Speed Tests for Genetic Mutations," *Washington Post*, November 24, 1997, A03; Collins, "Medical and Societal Consequences of the Human Genome Project," 33.

[102] For a discussion of nucleic acid hybridization, see page 32, this chapter.

device that reads the pattern of fluorescence for the thousands of testing spots. A computer program converts this information into DNA base pair sequence information.[103]

High start-up and chip costs have been a barrier to broader use of DNA chips.[104] However, commentators predict that, similar to electronic microchips, the capacity of DNA chips will continually increase, leading eventually to speedy, affordable, and comprehensive analysis of very large segments of an individual's genome.[105] One commentator predicts that soon, DNA chips will be able to test for 120,000 data points in a single test, an increased capacity of four orders of magnitude from just a few years ago.[106] The challenges to this approach are to develop almost absolute levels of accuracy and higher levels of test throughput.[107]

Some investigators are designing DNA microarrays for another approach, called genetic expression profiling.[108] This approach does not detect inherited mutations. Instead, it analyzes tissue mRNA samples to determine which of tens of thousands of the human genome are expressed ("turned on") in particular normal or diseased tissues.[109] It also can detect quantitative differences in the levels of gene expression. These differences can provide useful information about the role of specific genes in complex disorders. They also might point out new genetically based drug development approaches. Currently, researchers are developing microarray technology for clinical diagnosis of particular types of cancer. Some identified cancer-associated changes in gene expression are informative about prognosis and potential response to treatment options.[110] This approach represents an exponential increase in genetic testing capacity over other existing technologies.

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[103] Brown, "DNA-Encoded Chips," A03; see also Gene-Chips website: *http://www.gene-chips.com*, visited October 1, 1999.

[104] Shi, Bleavins, and de la Iglesia, "Technologies for Detecting Genetic Polymorphisms," 349.

[105] Collins, "Medical and Societal Consequences of the Human Genome Project," 33; see also "The Chipping Forecast," *Nature Genetics* 21 suppl. (1999); A. P. Shuber et al., "High Throughput Parallel Analysis of Hundreds of Patient Samples for More Than 100 Mutations in Multiple Disease Genes," *Human Molecular Genetics* 6 (1997): 337; Fisher, "Biology Meets Technology."

[106] C. Sander, "Genomic Medicine and the Future of Health Care," *Science* 287 (2000): 1977.

[107] Fisher, "Biology Meets Technology."

[108] R. L. Strausberg, "Genetics in Profile," *Trends in Genetics* 14 (1998): 50; van Ommen, Bakker, and den Dunnen, "The Human Genome Project and the Future of Diagnostics," 7–8.

[109] Investigators make a "cDNA microarray" with testing spots that contain representative, invariant segments of many thousands of different genes. The sample probes that are washed over the microarray consist not of genomic DNA, but cDNA (complementary DNA) samples, prepared from mRNA samples. Specific binding of labeled sample cDNA to different testing spots on the chip generates detailed information about which genes are expressed in a tissue sample.

[110] C. Theillet, "Full Speed Ahead for Tumor Screening," *Nature Medicine* 4 (1998): 767; see also J. Stephenson, "Human Genome Studies Expected to Revolutionize Cancer Classification," *Journal of the American Medical Association* 282 (1999): 927.

### Mass Spectrometric DNA Analysis

A very different approach to DNA sequence analysis provides another potential direction for more comprehensive genetic testing. Some claim this technique, mass spectrometry (MS), combines the DNA chip's speed with exquisite accuracy.[111] A mass spectrometer vaporizes a DNA sample and accelerates the molecules through a vacuum chamber. Scientists measure the small differences in time required for different sample molecules to move through the chamber. These differences translate into differences in molecular mass as small as 0.03 percent, which indicate differences in base pair sequence.[112]

MS has high specificity and accuracy and does not require the use of special probes and primers.[113] Although this technology has not yet been generally applied, several companies are developing mass spectrometric applications for clinically relevant human gene variants. The technique, similar to the DNA chip method, also can be adapted to analyze changes in specific gene expression. A current barrier to broader use of MS is its limited sample input capacity and requirement for highly purified samples.[114]

### Tandem Mass Spectrometry for Metabolite Analysis

Another application of mass spectrometric analysis, tandem mass spectrometry (TMS), is used for detection of metabolic disorders by phenotypic analysis of metabolites in blood and other body fluids. TMS uses two mass spectrometers in sequence (in "tandem"). The first separates molecular components of the blood or body tissue sample by molecular mass; these components are then fragmented. The second spectrometer analyzes the molecular masses of the fragments of each component, producing a specific molecular identity.[115] Some call TMS a "sea change" in testing methods for newborn screening and claim that it allows very sensitive, reliable, and affordable testing for multiple disorders in a single test.[116]

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[111] J. Alper, "Weighing DNA for Fast Genetic Diagnosis," *Science* 279 (1998): 2044; Leonard, "The Future of Molecular Genetic Testing," 729; Anthony V. Carrano, Ph.D., Director, Biology and Biotechnology Research Program, Lawrence Livermore National Laboratories, presentation at "The Implications of Individualizing Medicine through Genomics," Stanford University Program in Genomics, Ethics, and Society, October 17, 1998.

[112] Thus, it can detect any variation in a particular DNA segment, rather than only specific variations (as with chip technology).

[113] Shi, Bleavins, and de la Iglesia, "Technologies for Developing Genetic Polymorphisms," 349.

[114] Ibid.

[115] A. Berger, "Commentary — What Is Tandem Mass Spectrometry?" *British Medical Journal* 319 (1999): 477.

[116] H. L. Levy, "Newborn Screening by Tandem Mass Spectrometry: A New Era," *Clinical Chemistry* 44 (1998): 2401; see also Chapter 6, page 164.

# 3

## Predictive Genetic Testing

Predictive genetic testing includes reproductive testing and late-onset testing of healthy adults to determine future disease risks.[1] For both types of testing, new gene discoveries and testing technologies continue to expand the number and range of tests available.[2]

Generally, individuals seek or are offered reproductive or late-onset predictive genetic testing to reduce the risk of future disease or disability. One commentator distinguishes between two forms of prevention that generally correspond to these two types of testing.[3] Genotypic prevention aims to prevent the conception or birth of a person with a particular genotype, for example, by carrier or prenatal testing for Tay-Sachs disease. Phenotypic prevention aims to prevent the manifestation of a health risk linked to one or more inherited genetic variants in the person tested. An example of phenotypic prevention is altered lifestyle, heightened medical surveillance, or medical intervention to prevent a particular disease. Apart from these preventive goals, individuals may seek predictive genetic testing to reduce uncertainty about the future.

In recent years, new applications of predictive genetic testing also are being developed. These include testing for inherited gene variants, sometimes called "biomarkers," which can be used to guide an individual's pharmaceutical treatment (pharmacogenetic biomarkers) or to detect elevated health risk for exposures to specific environmental agents (biomarkers of susceptibility).[4]

### Reproductive Testing

Before the 1960s, testing for reproductive risk for genetic disease did not exist. Couples who knew, based on family history, that they were at risk for bearing a child with a genetic disorder could either accept the risk of having an affected child or refrain from attempting to conceive.[5] This began to change in the 1960s and 1970s, with the advent of fetal cell testing by amniocentesis and the legalization of abortion.[6]

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[1] Newborn testing, another form of predictive genetic testing, is administered by state screening programs and is considered separately in Chapter 6.

[2] See Chapter 2.

[3] E. T. Juengst, "Caught in the Middle Again: Professional Ethical Considerations in Genetic Testing for Health Risks," *Genetic Testing* 1 (1997/1998): 189, 197; see also Chapter 2, page 30.

[4] See pages 73–75, this chapter.

[5] See C. G. Gauthier, "The Impact of Recombinant DNA Technology on Genetic Screening," *Public Affairs Quarterly* 3 (1989): 25.

[6] *Roe v. Wade*, 410 U.S. 113 (1973).

Today, new gene discoveries, developments in DNA-based and cytogenetic testing, and techniques for monitoring fetal status present prospective and expectant parents with a broad range of available testing.[7] Reproductive genetic testing includes: (1) carrier testing of individuals who intend to reproduce or who have already initiated a pregnancy, (2) prenatal testing of fetal cells, and (3) pre-implantation testing of embryos created by in vitro fertilization (IVF).[8] It also includes investigational procedures for preconception selection of sperm.

### Carrier Testing

Carrier testing aims to identify individuals at increased risk for transmitting genetic disorders to future offspring. It may be targeted to individuals based on family history of a single-gene disorder, including autosomal recessive disorders such as Tay-Sachs disease, X-linked disorders such as Becker muscular dystrophy, and autosomal dominant disorders such as Huntington disease. Carrier testing also is performed as a population screening test, targeted at individuals of a particular racial, ethnic, or geographic population that is known to be at increased risk for a particular autosomal recessive disorder.[9] Examples include screening of African Americans for sickle cell disease carrier status and of persons of Ashkenazi Jewish descent for Tay-Sachs disease carrier status. In the past decade, rapid developments in gene discovery and testing technology have expanded the list of disorders for which carrier testing is available. Examples of disorders for which carrier testing only became available following gene discoveries and development of DNA-based tests include cystic fibrosis and Canavan disease, a serious and incurable metabolic disorder.[10]

Carrier testing may be performed as a preconception test, for individuals considering marriage or pregnancy. It also may be performed as a prenatal test, in which a pregnant woman and/or her partner is tested to determine whether or not an already conceived fetus is at risk; in this case, it is called a prenatal carrier test. If a woman is at risk for an autosomal dominant or X-linked disease, there is no need to test her partner. If both she and her partner are at risk for an autosomal recessive disease because of family history or ethnic or racial background, both partners may need to be tested.[11]

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[7] See I. B. Van den Veyver and B. B. Roa, "Applied Molecular Genetic Techniques for Prenatal Diagnosis," *Current Opinions in Obstetrics and Gynecology* 10 (1998): 97.

[8] For an overview of in vitro fertilization and other techniques, see The New York State Task Force on Life and the Law, *Assisted Reproductive Technologies: Analysis and Recommendations for Public Policy* (New York: New York State Task Force on Life and the Law, 1998).

[9] For a discussion of carrier screening, see Chapter 5, page 112.

[10] For both cystic fibrosis and Canavan disease, the only reliable form of carrier testing is by DNA-based testing. See J. R. Riordan et al., "Identification of the Cystic Fibrosis Gene: Cloning and Characterization of Complementary DNA," *Science* 245 (1989): 1066; R. Kaul et al., "Cloning of the Human Aspartoacylase cDNA and a Common Missense Mutation in Canavan Disease," *Nature Genetics* 5 (1993): 118; R. Matalon and K. Michals-Matalon, "Prenatal Diagnosis of Canavan Disease," *Prenatal Diagnosis* 19 (1999): 669. For a discussion of cystic fibrosis carrier screening, see Chapter 5, page 116.

[11] In some cases, the health care provider will test the woman first and only test her partner if she tests positive for a mutation. In other cases, providers may test both partners simultaneously. For late-onset

## Prenatal Testing

### *Genetic Testing of Fetal Cells*

#### *Invasive Fetal Cell Testing*

Fetal cells may be obtained and tested directly to assess risk for genetic or chromosomal disorders. To obtain a fetal cell sample, a physician can use one of two invasive techniques, amniocentesis or chorionic villus sampling (CVS). For amniocentesis, a physician removes a small volume of amniotic fluid by needle aspiration at sixteen weeks of pregnancy or earlier.[12] For CVS, a physician passes a catheter through the cervix and into the pregnant uterus and removes a sample of chorionic tissue, which develops from but is separate from the fetus. CVS can be performed earlier than amniocentesis, at nine to twelve weeks of pregnancy.[13] Both techniques are invasive and carry a significant but small risk of inducing miscarriage.[14]

Fetal cell analysis may be offered to couples whose fetus is at a known risk for a single-gene disorder. For example, testing may be offered as a follow-up to prenatal carrier testing when both members of a couple are identified as carriers of a mutation for an autosomal recessive disease.[15] In such cases, fetal cells are analyzed by DNA-based or biochemical techniques.[16]

The most frequent reason for fetal cell testing, however, is for the detection of chromosomal abnormalities by cytogenetic analysis.[17] The incidence of chromosomal abnormalities in pregnancy is high, accounting for half or more of spontaneous miscarriages and occurring in 0.5 percent of newborns.[18] They include alterations in chromosome number (e.g., Down syndrome, caused by inheriting an extra copy of chromosome 21) or structure.[19] In both cases, affected individuals may acquire or lose a copy of one or many genes, generally resulting in a wide range of physical and/or mental impairments.[20] Unlike gene mutations inherited from one generation to the next,

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dominantly inherited diseases, e.g., Huntington disease, it also is possible that the father is the potential carrier and the person who should be tested.

[12] T. D. Gelehrter, F. S. Collins, and D. Ginsburg, *Principles of Medical Genetics*, 2d ed. (Philadelphia, PA: Williams and Wilkins, 1997), 298.

[13] Ibid., 300. The two techniques have equal diagnostic accuracy and similar costs. Amniocentesis also provides diagnostic information about neural tube defects, based on measurement of alpha-fetoprotein levels in the amniotic fluid.

[14] See page 57, this chapter.

[15] In this case, the chance of an affected pregnancy is 25 percent.

[16] See Chapter 2.

[17] See Chapter 2, page 38.

[18] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 153, 169. About 15 percent of recognized pregnancies end in spontaneous miscarriage. The authors estimate at least 25 percent of conceived pregnancies have major chromosomal abnormalities.

[19] For a discussion, see Chapter 1, page 20.

[20] For example, individuals with Down syndrome have three copies, rather than the normal two copies, of over 1,000 genes located on chromosome 21.

chromosomal abnormalities usually occur during gamete (egg and sperm) cell development and appear spontaneously within families. Chromosomal abnormalities are more common with increasing maternal age.[21] Based on this risk, testing generally is offered to pregnant women who will be age thirty-five or older at the time of birth.[22]

*Testing of Fetal Cells from Maternal Blood*

During pregnancy, small numbers of fetal cells may be released into the maternal bloodstream, and some evidence suggests that higher numbers may be released in fetuses with chromosomal abnormalities.[23] These findings, along with the ability to perform genetic testing on very limited cell numbers, provide the basis for attempts to perform noninvasive fetal cell testing by maternal blood analysis. These attempts are at an investigational stage and face significant challenges.[24] Some suggest, however, that testing of fetal cells from maternal blood may be used as a screening test, perhaps in conjunction with maternal serum marker testing and ultrasonography, for detecting pregnancies at risk for Down syndrome.[25] In the United States, the National Institutes of Health is sponsoring a multicenter clinical trial to further evaluate maternal fetal cell testing.[26]

### *Maternal Serum Screening*

Maternal serum screening is a noninvasive and indirect method to obtain risk information about fetal development. It is based on analysis of a maternal blood sample obtained at a defined period in early pregnancy to determine serum concentration of three biochemical components.[27] The multiple marker screening test, also called the "triple

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[21] For example, the incidence of Down syndrome births, caused by inheritance of an extra copy of chromosome 21, is 1 in 1,250 for a twenty-five-year-old woman and 1 in 106 for a forty-year-old woman. March of Dimes, *Fact Sheet: Down Syndrome*, March of Dimes website: *http://www.modimes.org*, visited August 18, 1999.

[22] At this age, the risk of a chromosomal abnormality is equal to the risk of inducing a miscarriage. For a discussion of prenatal testing offered as a screening test, see Chapter 5, page 109.

[23] For a discussion, see D. W. Bianchi, "Fetal Cells in Maternal Circulation: Feasibility for Prenatal Diagnosis," *British Journal of Haemotology* 105 (1999): 574.

[24] See C. D. Steele et al., "Prenatal Diagnosis Using Fetal Cells Isolated from Maternal Peripheral Blood: a Review," *Clinical Obstetrical Gynecology* 39 (1996): 801.

[25] Ibid.

[26] The study is known as NIFTY (National Institutes of Health FeTal Cell StudY). See F. de la Cruz et al., "Prenatal Diagnosis by Use of Fetal Cells Isolated from Maternal Blood," *American Journal of Obstetrics and Gynecology* 173 (1995): 1354; Van den Veyver and Roa, "Applied Molecular Genetic Techniques," 101; Bianchi, "Fetal Cells in Maternal Circulation," 579. Based on preliminary data analysis, Bianchi reports that detection of chromosomal abnormalities is 40 to 50 percent with a false positive rate of 1 percent, considerably lower than the 5 percent false positive rate for maternal serum marker analysis.

[27] See American College of Obstetricians and Gynecologists, *Maternal Serum Screening* (Educational Bulletin 228, September 1996). The test is offered at sixteen to eighteen weeks of pregnancy. Recent articles discuss research aimed at earlier testing and improved specificity of multiple marker testing and combined marker testing and ultrasonography for detection of Down syndrome. See J. E. Haddow et al.,

screen," does not meet the definition of a precise genetic test — it does not provide specific information about the form or number of a particular gene or chromosome.[28] Rather, this screening test identifies from a large population of pregnant women a smaller group that is at increased risk of certain fetal disorders and who may benefit from a more specific test.[29] The disorders indicated are neural tube defects,[30] Down syndrome, and trisomy 18. Measure of the three serum components in pregnant women under age thirty-five can detect up to 60 percent of Down syndrome cases[31] and 85 percent or more of neural tube defects within this population.[32]

### *Ultrasonography*

Ultrasonography is a noninvasive technique that uses ultrasound imaging technology to generate fetal images during pregnancy.[33] It is commonly performed to assess gestational age, monitor fetal growth, and detect multiple pregnancies. It is used as a guide to the staging of maternal serum testing and invasive testing techniques; it also serves as a surgical guide for the latter techniques.

Ultrasonography also is a sensitive tool for the diagnosis of congenital fetal anatomical abnormalities which often are not caused by chromosomal or single-gene abnormalities.[34] It is not a specific genetic test, but, like maternal serum testing, it is now used routinely as a screening test for fetal anomalies. Targeted ultrasound is indicated as a follow-up to abnormal maternal serum testing. Ultrasound findings of characteristic congenital abnormalities may indicate chromosomal abnormalities and are generally followed by amniocentesis and cytogenetic testing.[35]

## Pre-implantation Genetic Testing of Embryos

Assisted reproductive technologies allow couples to overcome infertility through a variety of techniques, including IVF, in which a woman's eggs are retrieved and mixed with a

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"Screening of Maternal Serum for Fetal Down's Syndrome in the First Trimester," *New England Journal of Medicine* 338 (1998): 955; B. J. Wald, H. C. Watt, and A. K. Hackshaw, "Integrated Screening for Down's Syndrome Based on Tests Performed during the First and Second Trimester," *New England Journal of Medicine* 341 (1999): 461. For a discussion of ultrasonography, see page 53, this chapter.

[28] For a definition of genetic testing, see Chapter 2, page 29.

[29] American College of Obstetricians and Gynecologists, *Maternal Serum Screening*.

[30] For a discussion of neural tube defects, see March of Dimes, *Fact Sheet: Spina Bifida*, March of Dimes website, *http://www.modimes.com/HealthLibrary2/factsheets/Spina_Bifida.htm*, visited August 18, 1999.

[31] Although risk for chromosomal abnormalities, including Down syndrome, rises with advancing maternal age, there are a greater number of births for women under age thirty-five and, therefore, about 80 percent of all Down syndrome pregnancies occur in this population. See D. N. Saller and J. C. Canick, "Maternal Serum Screening for Fetal Down Syndrome: Clinical Aspects," *Clinical Obstetrics and Gynecology* 39 (1996): 783, 784.

[32] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 292; Dr. Harry Ostrer, Human Genetic Program, New York University Medical Center, personal communication.

[33] Ibid., 301; March of Dimes, *Fact Sheet: Ultrasound*, March of Dimes website, visited August 18, 1999.

[34] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 301. The authors state that the sensitivity and specificity for ultrasonagraphic detection of congenital anomalies is 95 percent. Some detectable congenital disorders are caused by environmental factors or a complex interplay of multiple genetic and/or environmental factors.

[35] For example, ultrasound assessment of the increased fluid-filled space at the back of the fetal neck, called the nuchal translucency measurement, can detect a majority of Down syndrome fetuses. See R. J. M. Snijders et al., "U. K. Multicentre Project on Assessment of Risk of Trisomy 21 by Maternal Age and Nuchal-Translucency Thickness at 10–14 Weeks of Gestation," *The Lancet* 351 (1998): 343.

male partner's sperm in a laboratory dish.[36] After several days of culture, some or all of the embryos are transferred into the prospective mother's uterus.[37] This technology, coupled with genetic testing techniques that require only a single cell, allows practitioners to remove and test a single cell from each embryo for genetic diagnosis.[38] Practitioners can test individual cells for particular gene variants by polymerase chain reaction (PCR) analysis[39] or for chromosomal abnormalities by cytogenetic FISH analysis.[40] Embryos that test positive for a gene mutation or chromosomal abnormality would not be transferred. This procedure, called pre-implantation genetic diagnosis (PGD), was first introduced in 1989 to enable couples at genetic risk to establish healthy pregnancies and avoid the need for pregnancy termination decisions based on prenatal testing results.[41]

In a 1999 article, a PGD practitioner reported that approximately 200 healthy infants had been born following PGD at more than 40 sites worldwide.[42] PGD has been used to avoid transferring embryos affected by known single-gene disorders such as cystic fibrosis and Tay-Sachs disease.[43] For cases involving couples at risk for X-linked disorders for which no familial gene mutation has been identified, practitioners have used PGD to select only female embryos.[44] The majority of PGD procedures have been performed to detect chromosomal abnormalities, and a recent report cites a "tendency of wider use of PGD" for IVF procedures involving women of advanced maternal age, who are at higher risk for such abnormalities. [45] Despite the success

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[36] For a discussion of assisted reproductive technologies, see New York State Task Force on Life and the Law, *Assisted Reproductive Technologies*.

[37] Generally, more embryos form than can be transferred in one cycle and remaining embryos may be frozen for transfer at a later cycle.

[38] See S. J. Faouliotis and J. G. Schenker, "Preimplantation Genetic Diagnosis Principles and Ethics," *Human Reproduction* 13 (1998): 2238; A. McLaren, "Genetics and Human Reproduction," *Trends in Genetics* 14 (1998): 427; R. J. Tasca and M. E. McLure, "The Emerging Technology and Application of Preimplantation Genetic Diagnosis," *Journal of Law, Medicine, and Ethics* 26 (1998): 7. An indirect variation of this technique that also is used is based on analysis of polar bodies, components that are extruded from the egg as byproducts of meiosis and which contain the portion of the egg's original chromosome complement that is not transmitted to the embryo. See Y. Verlinsky et al., "Prepregnancy Testing for Single-Gene Disorders by Polar Body Analysis," *Genetic Testing* 3 (1999): 185. For a discussion of meiosis, see Chapter 1, page 8.

[39] See Chapter 2, page 34.

[40] See Chapter 2, page 39.

[41] See Y. Verlinsky, "Preimplantation Diagnosis: An Alternative to Prenatal Diagnosis of Genetic and Chromosomal Disorders," *Journal of Assisted Reproduction and Genetics* 16 (1999): 161; American Society for Reproductive Medicine, *Fact Sheet: Preimplantation Genetic Diagnosis*, 1998, American Society of Reproductive Medicine website: *http://www.asrm.org/fact/preimpl.html*, visited November 25, 1998.

[42] Verlinsky, "Preimplantation Diagnosis," 164.

[43] American Society for Reproductive Medicine, *Fact Sheet: Preimplantation Genetic Diagnosis.*

[44] Ibid. Generally, girls are not at risk for X-linked disorders, while boys are at 50 percent risk. See Chapter 1, page 17.

[45] Verlinsky, "Preimplantation Diagnosis," 161–162. The author cites data for increased rate of embryonic chromosome abnormalities in women of advanced maternal age using IVF, "demonstrating the clinical significance of the procedure for improving the chances of IVF patients to become pregnant."

stories, PGD still faces significant technical challenges, as well as low pregnancy rates and the high financial and emotional costs associated with IVF.[46]

### Sperm Selection

One commercial laboratory offers a procedure called MicroSort, which enriches semen samples for sperm cells that contain either an X chromosome or a Y chromosome, allowing couples to increase the chance of having a child of a particular sex.[47] This procedure is offered to couples at risk for transmitting an X-linked disorder to increase their chance of having a girl.[48] It also is offered to couples who already have at least one child and wish to have a "balanced" family.[49]

The procedure requires treatment of the semen sample with a DNA-binding dye and analysis of the treated samples by a machine called a flow cytometer. The machine passes each treated sperm cell in the sample by a laser, which generates a quantitative signal based on the DNA content of the cell. Sperm cells with an X chromosome contain slightly more DNA than those with a Y chromosome, allowing the machine to "sort" the sample into two samples, one enriched for X sperm and one enriched for Y sperm. Enriched samples are used for intrauterine insemination or IVF to increase the chance of producing a female or male offspring. MicroSort cannot guarantee the desired outcome — it reportedly provides an 85 percent X chromosome sperm sample and a somewhat less enriched Y chromosome sperm sample.[50] The procedure is still investigational.[51]

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[46] Fasouliotis and Schenker, "Preimplantation Genetic Diagnosis Principles and Ethics," 2244; McLaren, "Genetics and Human Reproduction," 428; J. R. Botkin, "Ethical Issues and Practical Problems in Preimplantation Genetic Diagnosis," *Journal of Law, Medicine, and Ethics* 26 (1998): 17, 26.

[47] E. F. Fugger et al., "Birth of Normal Daughters after MicroSort Sperm Separation and Intra-Uterine Insemination, In Vitro Fertilization, or Intracytoplasmic Sperm Injection," *Human Reproduction* 13 (1998): 2367.

[48] Generally, girls are not at risk for X-linked disorders, while boys are at 50 percent risk. See Chapter 1, page 17.

[49] Fugger et al., "Birth of Normal Daughters after MicroSort Sperm Separation," 2368, 2369.

[50] Ibid. In this study, 88.2 percent of fetuses in established pregnancies were female. See also L. Belkin, "Getting the Girl," *New York Times Magazine*, July 25, 1999, at New York times website: *http://www.nytimes.com/library/magazine/home/19990725mag-sci-gender-choice.html*, visited July 26, 1999. The article claims that the success rate is 93 percent for producing girls and 73 percent for producing boys.

[51] See Fugger et al., "Births of Normal Daughters," 87; J. L. Simpson and S. A. Carson, "The Reproductive Option of Sex Selection," *Human Reproduction* 14 (1999): 870, 871. There are potential safety concerns based on the possibility of damage to sperm cell DNA (and resulting progeny) due to binding of the dye and exposure to a laser, potentially increasing the chance of mutation. There is no evidence for safety problems in animal studies and the commentators opine that potential safety problems are surmountable.

## Benefits and Risks of Reproductive Testing

### *Benefits of Testing*

#### *Expanded Reproductive Options*

Reproductive testing expands options for reproductive planning and decision-making. Some individuals may choose to exercise these options for marital as well as reproductive decision-making.[52] More commonly, individuals and couples use predictive testing to inform decisions about whether and how to initiate and continue pregnancies. Couples at reproductive risk for serious disorders, such as Tay-Sachs disease, who may otherwise have foregone pregnancy, may use reproductive testing to promote the birth of a healthy child.[53] Couples that are at risk for transmitting an X-linked disorder and who previously may have terminated any male pregnancy, due to the 50 percent chance that the fetus would inherit the disorder, may use reproductive testing to prevent termination of a healthy male pregnancy.[54] Individuals who would not consider abortion or who have experienced repeated miscarriages or pregnancy terminations based on prenatal test results may choose IVF and pre-implantation genetic diagnosis of embryos.

#### *Reduced Morbidity and Mortality*

Reproductive testing enables the prevention of births of infants with severe disease and disability. One example is the prevention of infants affected by Tay-Sachs disease, a progressive neurodegenerative disease that is uniformly fatal within several years of birth.[55] Voluntary carrier screening and prenatal testing from 1970 to 1993 led to a greater than 90 percent reduction in the annual number of infants diagnosed with Tay-Sachs disease within the Ashkenazi Jewish communities of the United States and Canada.[56]

In limited cases, reproductive fetal diagnosis permits prenatal medical intervention to prevent or decrease morbidity. For example, prenatal diagnosis of congenital adrenal hyperplasia by DNA-based testing enables prenatal treatment to prevent the development of ambiguous genitalia in affected females.[57] The treatment, administration of a steroid

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[52] For example, see Chapter 5, page 112.

[53] See M. Kabach et al., "Tay-Sachs Disease — Carrier Screening, Prenatal Diagnosis, and the Molecular Era," *Journal of the American Medical Association* 270 (1993): 2307, 2309.

[54] Gauthier, "The Impact of Recombinant DNA Technology," 33.

[55] See Chapter 2, page 40.

[56] Kabach, "Tay-Sachs Disease — Carrier Screening," 2309–2310; see also F. Kaplan, "Tay-Sachs Disease Carrier Screening: A Model for Prevention of Genetic Disease," *Genetic Testing* 2 (1998): 271. Before 1970, about 60 new cases per year were diagnosed; from 1983 to 1993, this declined to 2 to 3 cases per year. The incidence of Tay-Sachs disease was about a hundred-fold higher for the Jewish versus the general population. For a discussion of Tay-Sachs disease carrier screening programs, see Chapter 5, page 112.

[57] A. D. Carlson et al., "Congenital Adrenal Hyperplasia: Update on Prenatal Diagnosis and Treatment," *Journal of Steroid Biochemistry and Molecular Biology* 69 (1999): 19.

hormone to the woman carrying the affected fetus, is safe for fetuses and pregnant women and can prevent the need for genital surgery, sex misassignment, and gender confusion.[58]

### *Reduction of Anxiety*

For individuals at reproductive risk for an affected pregnancy based on family history, reproductive testing that provides a negative result (no evidence for the mutant gene variant) can reduce or eliminate anxiety that might otherwise persist through pregnancy and even through infancy. For women of advanced maternal age, prenatal test results may prevent concerns about fetal chromosomal abnormalities.

### *Information to Prepare for a Birth*

In some cases, individuals or couples who undergo prenatal testing may learn that their fetus is affected by a genetic condition or chromosomal abnormality and choose to continue the pregnancy. Earlier knowledge about their future child's medical condition may allow them, with their physician, to plan birth conditions (for example, birth at a tertiary care center with medical specialists standing by) to optimize the infant's medical treatment. Families also may use this information for emotional and practical preparation, for example, to prepare for special educational and other support needs.[59]

## ***Risks of Testing***

### *Harm to the Fetus*

Invasive prenatal testing poses a small risk of inducing miscarriage. The rate for miscarriage following amniocentesis is less than 1 in 200; for CVS, between 1 and 2 in 100.[60]

### *Inaccurate Test Results*

For carrier and prenatal testing, there is a small risk that individuals and couples may receive inaccurate or incorrect test results caused by errors in test performance, sample mix-ups, or record-keeping. For example, in a survey of worldwide prenatal diagnoses for Tay-Sachs disease from 1969 to 1992 involving 2,416 pregnancies, three fetuses affected by Tay-Sachs disease were misdiagnosed as unaffected.[61] Errors in carrier testing for Tay-Sachs also

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[58] Ibid.

[59] D. Wertz and R. Gregg, "Optimizing Genetics Services on a Social, Ethical, and Policy Context: Suggestions from Consumers and Providers in the New England Regional Genetics Group," *The Genetic Resource* 10, no. 2 (1996): 49.

[60] The risk may be lower for more experienced practitioners. March of Dimes, *Fact Sheet: Chorionic Villus Sampling*, March of Dimes website, visited August 18, 1999.

[61] National Institutes of Health-Department of Energy (NIH-DOE) Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of

have occurred and resulted in at least fifteen major lawsuits.[62] In pre-implantation testing of embryos, technical challenges have resulted in some incorrect diagnoses, leading to the birth of affected infants.[63]

### *Potential of Discrimination*

Results of a carrier test might subject an individual to the adverse use of genetic information in insurance or employment decisions, even though carriers are themselves generally free of health impairments.[64] For example, in the 1970s, individuals identified as carriers for sickle cell disease were subjected to insurance, workplace, and school-based discrimination based on faulty and misapplied information.[65]

## *Increased Anxiety and Difficult Choices*

Prenatal test results may not be clear-cut and may provoke anxiety for pregnant women and couples. The prenatal testing process and associated anxiety may interfere with maternal acceptance of the pregnancy and maternal bonding to the unborn child, creating what one commentator refers to as the "tentative pregnancy."[66]

Prenatal testing of fetal cells also can result in unclear diagnoses that may require difficult decision-making. For example, cytogenetic testing sometimes identifies alterations in chromosome structure that may or may not affect the health of the future infant.[67] The anxiety attendant to such diagnoses may be amplified when the couple tested expected a clear-cut "normal" or "abnormal" diagnosis.[68]

## *Eugenic Concerns*

Use of genetic testing to promote healthy births and to prevent the birth of infants affected by serious and incurable disorders can be considered a eugenic practice.[69] While most

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Health, 1997), 42 (quoting Dr. Michael M. Kabach, Director, International Tay-Sachs Disease Data Collection and Quality Control Program).

[62] Ibid.

[63] Tasca and McLure, "The Emerging Technology and Application of Preimplantation Genetic Diagnosis," 11–14; Y. Verlinsky and A. Kuliev, "Editorial: Preimplantation Genetics," *Journal of Assisted Reproduction and Genetics* 15 (1998): 215, 216. Verlinsky and Kuliev note that for a total of 166 healthy PGD births worldwide, four misdiagnoses also occurred and resulted in affected births. For a discussion, see W. Lissens and K. Sermon, "Preimplantation Genetic Diagnosis: Current Status and New Developments," *Human Reproduction* 12 (1997): 1756, 1757.

[64] For a discussion, see Chapter 9.

[65] H. Markel, "Scientific Advances and Social Risks: Historical Perspectives of Genetic Screening Programs for Sickle Cell Disease, Tay-Sachs Disease, Neural Tube Defects and Down Syndrome," in NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 161, 163–164; see also Chapter 5, page 115; see Chapter 10, page 281.

[66] B. Katz Rothman, *The Tentative Pregnancy: Prenatal Diagnosis and the Future of Motherhood* (New York: Viking, 1986).

[67] Ibid., 157–160.

[68] See K. McAuliffe, "A Little Knowledge, a Lot of Agony," *New York Times*, June 21, 1998, section 15, 22.

[69] For a discussion of eugenics, see Chapter 4, page 80. The original definition of eugenics does not require any systematic or coercive involvement of government or other entities, but, based on historical use of the term, many interpret it as such.

commentators find this practice acceptable for disorders such as Tay-Sachs disease, a serious neurodegenerative disorder that is fatal within the first few years of life, some voice concerns that expansion of available predictive tests will lead to inappropriate prenatal and/or pre-implantation selection against less serious genetic disorders.[70] As new tests continue to be developed, reproductive testing also will become increasingly available to detect gene variants that do not result in disease with 100 percent certainty (for example, BRCA testing for breast cancer susceptibility),[71] including variants that may increase risk for behavioral or cognitive disorders (for example, bipolar disorder)[72] or physical traits, including sex.[73]

Even for single-gene disorders present from birth, decisions to offer or use reproductive testing may not be straightforward. For example, the Institute of Medicine Committee on Assessing Genetic Risks pointed out that for certain single-gene disorders, the range and/or severity of symptoms can be very variable and that genetic testing generally cannot provide information about such variability.[74] Gaucher disease, for example, is an autosomal recessive disease with a wide range in severity; in fact, carrier screening programs have detected individuals who carry two mutant copies of the relevant gene but who have only mild or no symptoms.[75] While some commentators state that prenatal diagnosis should be offered only for serious genetic disorders and birth defects,[76] others point out that for individuals and couples, definitions of "serious" will

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[70] See, for example, President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions* (Washington, D.C.: U.S. Government Printing Office, 1983), 94; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 8, 166; R. Cook-Deegan, "Private Parts," *The Sciences*, March/April, 1994, 18; see also Botkin, "Ethical Issues and Practical Problems in Preimplantation Genetic Diagnosis," 23–24.

[71] J. M. Lancaster, R. W. Wiseman, and A. Berchuck, "An Inevitable Dilemma: Prenatal Testing for Mutations in the BRCA1 Breast-Ovarian Cancer Susceptibility Gene," *Obstetrics and Gynecology* 87 (1996): 306; T. M. U. Wagner and R. Ahner, "Prenatal Testing for Late-Onset Diseases such as Mutations in the Breast Cancer Gene 1 (BRCA1)," *Human Reproduction* 13 (1998): 1125.

[72] For a discussion of genetics and behavioral and cognitive traits, see Chapter 4, page 86.

[73] See page 55, this chapter. See also D. C. Wertz and J. C. Fletcher, "Ethical and Social Issues in Prenatal Sex Selection: A Survey of Geneticists in 37 Nations," *Social Sciences Medicine* 46 (1998): 255; Ethics Committee of the American Society of Reproductive Medicine, "Sex Selection and Preimplantation Genetic Diagnosis," *Fertility and Sterility* 72 (1999): 595.

[74] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 166.

[75] See D. Kronn, V. Jansen, and H. Ostrer, "Carrier Screening for Cystic Fibrosis, Gaucher Disease, and Tay-Sachs Disease in the Ashkenazi Jewish Population," *Archives of Internal Medicine* 158 (1998): 777, 779; see also J. Azuri et al., "Asymptomatic Gaucher Disease Implications for Large-Scale Screening," *Genetic Testing* 2 (1998): 297. Azuri et al. state that in Israel, gene frequency studies estimate there are 2,500 persons who have two mutant copies of the gene associated with Gaucher disease, but only 400 have been diagnosed. See also Chapter 5, page 130.

[76] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 8; E. R. Hepburn, "Genetic Testing and Early Diagnosis and Intervention: Boon or Burden?" *Journal of Medical Ethics* (1996): 105, 109.

vary,[77] that the availability of such services is inevitable,[78] and that "it will become impossible to enforce lines, even if they are drawn."[79]

Some commentators express concerns that an expanding range of conditions that will not be considered "bearable" will restrict concepts of what is "normal,"[80] that society will grow increasingly intolerant of disability,[81] and that parents, in search of their "designer child,"[82] will suffer disappointments when their expectations of such a child are not met.[83] Others point to societal harms posed by sex selection related to "unbalancing the sex ratio and perpetuating gender stereotyping."[84]

## Predictive Testing for Late-Onset Disorders

Not all genetic disorders manifest at birth or during infancy. Some single-gene and most complex disorders manifest later: during childhood, adolescence, or adulthood. Late-onset predictive testing aims to determine whether an asymptomatic individual has inherited a gene variant that increases risk for such a disorder.

Most commentators distinguish between two categories of late-onset predictive testing, based on the degree of certainty that an accurate genetic test can provide. "Presymptomatic" testing detects gene variants that lead to disease with 100 percent certainty, provided an individual lives long enough. "Susceptibility" (also referred to as "predispositional") testing has lower predictive value; test results provide relative risk information only.

Since genetic testing began, late-onset testing has comprised only a small percentage of predictive testing, and most of this has been presymptomatic testing for rare single-gene disorders. This is changing, however, because of the massive increase in information about gene variants that contribute to complex disorders such as cancer, heart disease, and some psychiatric disorders. Both presymptomatic and susceptibility testing may predict disease risk up to decades in advance of any symptoms, often in the absence of confirmed preventive or treatment interventions.

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[77] D. Wertz, "Drawing Lines: Notes for Discussion," in *Prenatal Testing for Genetic Disability*, ed. E. Parens (Washington, D.C.: Georgetown University Press, 2000).

[78] Hepburn, "Genetic Testing and Early Diagnosis," 109; A. Lippman, "Prenatal Genetic Testing and Screening: Constructing Needs and Reinforcing Inequities," *American Journal of Law and Medicine* 17 (1991): 15, 25; Wertz, "Drawing Lines."

[79] Wertz, "Drawing Lines."

[80] Lippman, "Prenatal Genetic Testing and Screening," 25.

[81] See J. L. Nelson, "The Meaning of the Act: Reflections on the Expressive Force of Reproductive Decision Making and Policies," *Kennedy Institute of Ethics Journal* 8 (1998): 165; D. Kaplan and M. Saxton, "Disability Community and Identity: Perceptions of Prenatal Screening," *Gene Watch* 12 (April, 1999): 4.

[82] Hepburn, "Genetic Testing and Early Diagnosis," 109.

[83] Ibid.; see also J. R. Botkin, "Prenatal Screening: Professional Standards and Limits of Parental Choice," *Obstetrics and Gynecology* 75 (1990): 875, 879.

[84] Wertz, "Drawing Lines."

### Presymptomatic Testing

Presymptomatic testing aims to detect mutant gene variants that confer a virtually 100 percent chance of developing a disorder. Perhaps the best known example is testing for Huntington disease, an autosomal dominant neurodegenerative disease that affects about 1 in 20,000 individuals.[85] Any person who has a parent with Huntington disease has a 50 percent chance of developing the disease later in life, based on whether they inherit the mutant versus the normal copy of the disease-associated gene from that parent. Symptoms generally begin in the fourth decade or later and result in progressive and severe mental deterioration and eventual death. Genetic testing to determine Huntington disease risk is prototypical of testing that can predict risk decades in advance of disease onset and in the absence of any preventive or treatment options.

The first genetic test to predict Huntington disease risk within affected families became available in 1983, after scientists identified a DNA marker that was co-inherited, or "linked," with development of the disease. Linkage testing is an indirect DNA-based testing method that traces disease-linked gene markers throughout affected families and predicts whether unaffected individuals are at increased or decreased risk for the family disorder; it does not provide a definitive positive or negative result.[86]

Because of the severity of Huntington disease, the lack of clinical interventions, and the limitations of linkage testing methods, the earliest genetic testing programs required extensive pretest and posttest counseling and follow-up.[87] Investigators worried that a test result indicating that a person was likely to develop Huntington disease might elicit catastrophic psychological responses. In fact, while a few individuals who learned that they were likely to develop the disorder did experience grave psychological distress, most did not.[88] In one study, one year after receiving a result highly predictive for the disease, most individuals showed a greater sense of psychological well-being than individuals who had not been tested and whose risk status remained uncertain.[89] Individuals informed that they most

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[85] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 217. See also Chapter 1, page 16.

[86] Linkage testing is performed when chromosomal markers known to be close to a yet unidentified gene are available. It is less reliable than direct DNA testing because even closely linked chromosome segments can segregate from generation to generation. It requires testing of symptomatic and asymptomatic family members and, based on analysis parameters, assigns a quantitative level of risk. See Chapter 2, page 36.

[87] S. Wiggins et al., "The Psychological Consequences of Predictive Testing for Huntington's Disease," *New England Journal of Medicine* 327 (1993): 1401.

[88] R. H. Meyers, "Direct Testing for Huntington's Disease," *The Genetic Resource* 8, no. 2 (1994): 5, 6. See also E. W. Almqvist et al., "A Worldwide Assessment of the Frequency of Suicide, Suicide Attempts, or Psychiatric Hospitalization after Predictive Testing for Huntington Disease," *American Journal of Human Genetics* 64 (1999): 1293. The 1999 study confirms that a small percentage of individuals respond catastrophically to a positive test result; see page 71, this chapter.

[89] Wiggins, "Psychological Consequences," 1404. The study involved 135 individuals. The "increased risk," "decreased risk," and "no change" groups contained 37, 58, and 40 individuals, respectively. The "no change" group contained self-selected individuals who either could not be tested (for example, due to unavailability of family members for testing) or chose not to be tested but agreed to participate in the study.

likely had not inherited the mutation also generally showed a psychological health benefit, although 10 percent reported serious difficulty in coping with the knowledge. Problems included facing an "unplanned future" and/or the realization that the test results did not confer power or resolve existing personal problems as expected. Both positive and negative test results enabled individuals to make life-planning decisions, including reproductive decisions.[90]

In 1993, scientists discovered the Huntington disease-associated gene, enabling development of a direct, PCR-based gene test.[91] The direct test can definitively determine whether an individual has inherited the mutated gene copy. The direct test also is less expensive than linkage testing, and it does not require testing of additional family members.[92]

### Susceptibility (Predispositional) Testing

Susceptibility tests detect gene variants that significantly increase an individual's risk for a particular disorder but not to the level of 100 percent. The effects of other genes and environmental factors influence the likelihood that a disease associated with a particular genetic susceptibility variant will develop. The predictive value of available gene tests varies accordingly. While many people think of predictive genetic tests as "crystal balls," one commentator has compared the predictive power of susceptibility tests to that of weather forecasts.[93]

Some commentators predict that susceptibility testing will be the most common type of genetic testing offered in the near future[94] and that, within a decade, physicians will routinely offer predictive genetic testing panels to determine an individual patient's future health risks.[95] Others, however, question the usefulness of susceptibility testing and express concerns about potential harms.[96] In addition to the potential harms posed by all late-onset genetic tests,[97] susceptibility testing raises special concerns because of the limited predictive power of tests, potential overemphasis on the meaning of test results,[98] and availability of testing before extensive population data have been collected.[99]

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[90] An accurate, direct DNA-based test now allows prenatal and pre-implantation testing. See pages 51 and 53, this chapter.

[91] The HD gene mutation is a trinucleotide repeat expansion (see Chapter 1, page 10). American College of Medical Genetics (ACMG)/American Society of Human Genetics (ASHG) Huntington Disease Genetic Testing Working Group, "ACMG/ACSG Statement: Laboratory Guidelines for Huntington Disease Genetic Testing," *American Journal of Human Genetics* 62 (1998): 1243. For a discussion of PCR, see Chapter 2, page 34.

[92] While disease prediction may be certain, age of onset varies significantly. For example, for individuals sharing an identical mutation of the huntingtin gene, recorded age of onset ranges from 28 to 66. Meyers, "Direct Testing for Huntington's Disease," 5, 6.

[93] Juengst, "Caught in the Middle Again," 191.

[94] J. Bell, "The New Genetics in Clinical Practice," *British Medical Journal* 316 (1998): 618.

[95] F. S. Collins, "Shattuck Lecture — Medical and Societal Consequences of the Human Genome Project," *New England Journal of Medicine* 341 (1999): 28, 34–35.

[96] See, e.g., S. Lehrman, "Predictive Genetic Testing: Do You Really Want to Know Your Future?" DNA Files website: *http://www.dnafiles.org/about/pgm4/topic.html*, visited November 25, 1998.

[97] See page 70, this chapter.

[98] See Chapter 4, page 91.

[99] See Chapter 2, page 43.

### *BRCA1 and BRCA2 Gene Mutation Testing*

Perhaps the best known example of susceptibility testing is for mutations in genes termed breast cancer susceptibility genes.[100] Two genes, BRCA1 and BRCA2, were discovered in 1994 and 1995, respectively.[101] Both genes were discovered by research involving families in which breast and/or ovarian cancer occurred at an unusually high incidence. This high cancer incidence suggested that within these families, inheritance of a single mutant gene variant conferred susceptibility to breast and/or ovarian cancer.[102]

DNA-based testing of both BRCA genes quickly became commercially available.[103] Both genes are very large and complex, and several hundred mutations have been identified for each. As a result, the test must scan, or "sequence," thousands of DNA bases of both genes.[104] Once a particular mutation is identified within a family, testing of additional family members can then "zero in" on that particular mutation. This approach also is used for testing in particular subpopulations that are at risk for inheriting one or more mutations known to be frequent within that group.[105] For example, women of Ashkenazi Jewish descent are known to be at significantly elevated risk for inheritance of one of three specific BRCA gene mutations.[106]

Although BRCA gene testing analyzes thousands of bases of both genes, it is subject to two major limitations of DNA-based genetic tests: (1) limited sensitivity (i.e., limited ability to detect all true positives) and (2) limited ability to predict whether inheritance of a particular gene

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[100] Although the BRCA genes are commonly termed "breast cancer susceptibility" genes, the normal versions of these genes play a role in the function of normal breast tissue. Cancer susceptibility is due to mutations that impair the function of these genes.

[101] For an overview of BRCA1 and BRCA2 genes, see G. B. Mann and P. I. Borgen, "Breast Cancer Genes and the Surgeon," *Journal of Surgical Oncology* 67 (1998): 267; S. L. Neuhauser and E. A. Ostrander, "Mutation Testing of Early-Onset Breast Cancer Genes BRCA1 and BRCA2," *Genetic Testing* 1 (1997): 75; 5; A. M. Martin and B. L. Weber, "Genetic and Hormonal Risk Factors in Breast Cancer," *Journal of the National Cancer Institute* 92 (2000): 1126; T. S. Frank, "Laboratory Determination of Hereditary Susceptibility to Breast and Ovarian Cancer," *Archives of Pathology and Laboratory Medicine* 123 (1999): 1023.

[102] Familial cases of breast and/or ovarian cancer account for 5 to 10 percent of all breast cancers. In some families, breast and/or ovarian cancer susceptibility appears as a single-gene trait. P. Kahn, "Coming to Grips with Genes and Risk," *Science* 274 (1996): 496; see also National Cancer Institute, "Genetics of Breast and Ovarian Cancer," National Cancer Institute website: *http://cancernet.nci.nih.gov/clinpdq/cancer_gen/*, visited August 16, 1999. Of families with three or more affected relatives, about two-thirds were found to have a mutation in either the BRCA1 (39 percent) or BRCA2 (25 percent) gene. C. I. Szabo and M. C. King, "Population Genetics of BRCA1 and BRCA2," *American Journal of Human Genetics* 60 (1997): 1013. See also D. Ford et al., "Genetic Heterogeneity and Penetrance Analysis of the BRCA1 and BRCA2 Gene in Breast Cancer Families," *American Journal of Human Genetics* 62 (1998): 676.

[103] In the text, BRCA will refer to both BRCA1 and BRCA2.

[104] Neuhauser and Ostrander, "Mutation Testing of Early-Onset Breast Cancer Genes"; Shen et al., "Novel Mutations in BRCA1 and BRCA2 Genes Detected by Automated High Throughput Sequencing," presentation at the Annual Meeting of the American Society of Human Genetics, Denver, CO, October 1998. For discussion of DNA sequencing, see Chapter 2, page 35.

[105] Frequent mutation incidence in a subpopulation is due to a "founder effect," which results from a rapid population expansion from a small ancestral group in which one or more ancestors carried a mutant gene. Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 343.

[106] Szabo and King, "Population Genetics," 1015. Researchers estimate that the frequency of each of these three BRCA gene mutations in the Ashkenazi Jewish population is close to 1 percent.

mutation will result in disease.[107] Limited sensitivity is caused by the inability of the test to detect all possible mutations that affect BRCA gene function, such as mutations that are "outside" the gene but that may affect the turning on and off of the gene.[108] One commentator estimated that testing could miss 5 to 15 percent of clinically significant BRCA gene mutations.[109] Also, current data suggest that mutations in other genes also may contribute to genetic susceptibility to breast cancer susceptibility.[110] Testing limited to BRCA1 and BRCA2 genes would not detect these susceptibility variants.

The second limitation is the uncertainty of prognostic risk information for specific mutations.[111] Some of the identified BRCA gene mutations clearly abolish or impair the function of the protein that is produced from the gene and thereby increase cancer risk.[112] However, other mutations, called genetic variants of "undetermined clinical importance," cause minor changes in the protein that may or may not affect its function or increase disease risk.[113] For women who are identified to have variants of undetermined clinical importance, follow-up studies are needed to determine whether these mutations increase cancer risk.[114]

Even for a particular mutation, the degree of disease risk may vary among individuals because of other genetic and environmental factors, such as pregnancy history, hormonal history, and exposure to toxic agents. For susceptibility testing, the degree of risk in the general population often is less than that for individuals in the unusually high-risk families in which the genes are discovered. Original research studies that led to the discovery of the two BRCA genes were performed in about 200 families that each had at least four members affected by breast and/or ovarian cancer. In these families, lifetime risk for breast cancer based on inheritance of a gene mutation was

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[107] See Chapter 2, page 43.

[108] Mutations occurring outside DNA coding regions (exons) would not be detected. See Chapter 1, page 9. Both BRCA genes have over twenty exons and introns. BRCA gene sequence analysis also will not detect large structural changes that occur in one gene copy. See Neuhauser and Ostrander, "Mutation Testing of Early-Onset Breast Cancer Genes," 76.

[109] D. Shattuck-Eidens et al., "BRCA1 Sequence Analysis in Women at High Risk for Susceptibility Mutations," *Journal of the American Medical Association* 278 (1997): 1242.

[110] For example, investigators believe that at least one more undiscovered gene accounts for a significant minority of high incidence breast cancer families. Szabo and King, "Population Genetics"; Ford, "Genetic Heterogeneity and Penetrance Analysis."

[111] P. Watson, J. N. Marcus, and H. T. Lynch, "Prognosis of BRCA1 Hereditary Breast Cancer," *The Lancet* 351 (1998): 304.

[112] Nonsense and frameshift mutations produce nonfunctional proteins. See Chapter 1, page 10.

[113] Frank, "Laboratory Determination of Hereditary Susceptibility to Breast and Ovarian Cancer," 1025.

[114] Missense mutations produce proteins with a single changed amino acid, which may or may not disrupt protein function. See Chapter 1, page 10. Myriad Genetics, a commercial testing laboratory, will record such mutations in its database for follow-up to determine clinical significance. Shen, "Novel Mutations in BRCA1 and BRCA2"; see also Myriad Genetics website*: http://www.myriad.com/0corp/labs/lab01b.html*, visited November 9, 1998.

calculated to be 87 percent.[115] For women with less extensive family history, however, the degree of lifetime cancer risk associated with inheritance of a mutation may be significantly lower.[116] For example, follow-up studies show that the three BRCA gene mutations that have an increased incidence in the Ashkenazi Jewish population confer a breast cancer risk estimated at 36 to 56 percent.[117] For most susceptibility tests, years of data collection and analysis are required to calculate reliable odds for different populations.[118]

Another complicating issue for BRCA gene testing is that, for women who test positive, posttest decisions about clinical preventive options can be difficult and complex. Options include heightened surveillance, prophylactic surgery to remove breast and/or ovarian tissue, and chemoprevention.[119] Heightened surveillance cannot eliminate future cancer risks, and many women who are at risk for familial cancer undergo increased monitoring regardless of genetic testing. Prophylactic surgery significantly reduces but does not eliminate future cancer risk and is a "major, irreversible step" that can have significant psychological, health, and social ramifications.[120] Prophylactic hormonal therapy, another option, also poses other health risks and lacks clear efficacy data for women who have BRCA gene mutations.[121]

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[115] Mann and Borgen, "Breast Cancer Genes," 267; B. Healy, "BRCA Genes — Bookmaking, Fortunetelling, and Medical Care," *New England Journal of Medicine* 336 (1997): 1448; see also Ford, "Genetic Heterogeneity and Penetrance Analysis," 676.

[116] A fact sheet issued by the National Action Plan for Breast Cancer and the National Cancer Institute states that lifetime breast cancer risk associated with inheritance of a BRCA1 or BRCA2 mutation is 50 to 85 percent, and "the risk for some women may be lower." National Action Plan on Breast Cancer and National Cancer Institute, *Fact Sheet: Genetic Testing for Breast Cancer Risk: It's Your Choice*, (Washington, D.C.: Government Printing Office, November 1997), 1; also available at the National Cancer Institute website: *http://rex.nci.nih.gov/NCI_PUB_INDEX_GENBRST/INDEX.HTM*, visited July 7, 2000. See also Mann and Borgen, "Breast Cancer Genes," 267.

[117] See Healy, "Bookmaking, Fortunetelling, and Medical Care"; J. Struewing et al., "The Risk of Cancer Associated with Specific Mutations of BRCA1 and BRCA2 among Ashkenazi Jews," *New England Journal of Medicine* 336 (1997): 1401; F. H. Fodor et al., "Frequency and Carrier Risk Associated with Common BRCA1 and BRCA2 Mutations in Ashkenazi Jewish Cancer Patients," *American Journal of Human Genetics* 63 (1998): 45. Another study of a single BRCA2 gene mutation that is frequent in the Icelandic population estimated lifetime breast cancer risk of 37 percent for those who carry the mutation. S. Thorlacius et al., "Population-Based Study of Risk of Breast Cancer in Carriers of BRCA2 Mutation," *The Lancet* 352 (1998): 1337.

[118] For example, the Cooperative Breast Cancer Registry, organized at the National Cancer Institute, is performing a multiyear clinical data collection on thousands of women with cancer and their relatives. Kahn, "Coming to Grips," 498.

[119] See D. Schrag et al., "Life Expectancy Gains from Cancer Prevention Strategies for Women with Breast Cancer and BRCA1 or BRCA2 Mutations," *Journal of the American Medical Association* 283 (2000): 617.

[120] See M. H. Frost et al., "Long-term Satisfaction and Psychological and Social Function following Bilateral Prophylactic Mastectomy," *Journal of the American Medical Association* 284 (2000): 319, 322.

[121] K. I. Pritchard, "Is Tamoxifen Effective in Prevention of Breast Cancer?" *The Lancet* 352 (1998): 80. Efficacy data are limited for the general population, as well as for the subpopulation of women with BRCA1 or BRCA2 gene mutations; the latter may be differentially responsive. See, e.g., Watson, Marcus, and Lynch, "Prognosis of BRCA1," 304.

### *Other Genetic Susceptibility Tests*

Other susceptibility tests cover a broad range of diseases, and the gene variants tested for contribute a variable range of risk. The test methods also vary considerably, from the extensive DNA sequencing of BRCA testing to detect any possible mutation to testing for one or a few identified population variants (alleles) that are linked to increased risk for certain disorders. The amount of clinical data that links a gene variant to a disease risk also varies. In some cases, the roles of secondary genetic and environmental factors involved in disease etiology have been identified. A few representative examples of genetic susceptibility tests are presented in this section.

#### *Hereditary Nonpolyposis Colorectal Cancer*

Hereditary nonpolyposis colorectal cancer (HNPCC) is a dominant disorder associated with familial colon cancer. Researchers estimate that 1 to 5 in 1,000 individuals carry a dominant mutation in one of six (or more) DNA repair, or "proofreader," genes that may lead to this disorder.[122] Individuals who inherit one of these mutations have a 70 to 80 percent chance of developing colon cancer in their lifetime, accounting for about 3 percent of the approximately 135,000 cases of colon cancer diagnosed annually in the United States.[123] Women who inherit a mutation also are at significant risk for endometrial cancer.[124] DNA-based testing is available for at least two of the genes associated with HNPCC. A positive genetic test identifies individuals who can benefit from periodic colonoscopic and other monitoring.[125]

### Alpha-1 Antitrypsin Deficiency

Alpha-1 antitrypsin deficiency is an autosomal recessive condition that places individuals at risk for emphysema, an adult-onset chronic lung disease.[126] Individuals who inherit two mutant copies of the alpha-1 antitrypsin gene have a twenty-fold or higher risk of developing emphysema than the general population. The likelihood that persons who inherit two mutant copies of this gene will develop emphysema depends largely on whether they smoke.[127] Smokers generally develop symptoms of emphysema

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[122] J. T. O'Leary, "Molecular Diagnostics of Hereditary Nonpolyposis Colorectal Cancer," *Journal of the American Medical Association* 282 (1999): 281. For a discussion of DNA repair genes, see Chapter 1, page 19.

[123] F. M. Giardiello, "Genetic Testing in Hereditary Colorectal Cancer," *Journal of the American Medical Association* 278 (1997): 1228.

[124] O'Leary, "Molecular Diagnostics of Hereditary Nonpolyposis Colorectal Cancer," 261.

[125] Cancer Genetics Studies Consortium, "Consensus Statement: Recommendations for Follow-up Care of Individuals with an Inherited Predisposition to Cancer I. Hereditary Nonpolyposis Colon Cancer," *Journal of the American Medical Association* 277 (1997): 915.

[126] For discussion of autosomal recessive disorders, see Chapter 1, page 16.

[127] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 125; see also World Health Organization, "Alpha-1 Antitrypsin Deficiency: Memorandum from a WHO Meeting," *Bulletin of the World Health Organization* 75 (1997): 397.

between ages thirty and forty, with a median age of death at fifty, while nonsmokers typically remain disease-free or develop milder disease later in life.[128]

In the Northern European population, approximately 1 in 2,500 individuals inherits two copies of identified susceptibility variants for alpha-1 antitrypsin deficiency, placing them at increased risk.[129] Predictive genetic testing is available, and some commentators suggest that a positive test result may give individuals a strong incentive to avoid cigarette smoking.[130]

*Apolipoprotein E Variants and Late-Onset Alzheimer Disease*

Apolipoprotein E (APOE) testing does not scan for every possible mutated variant of the APOE gene — it analyzes whether a person has inherited one or two copies of the three major population APOE gene variants.[131] Every individual has two copies of the APOE gene, generally one or two copies of any of the three most common forms, called APOE2, APOE3, and APOE4.[132] The protein produced from the APOE gene is present in the blood and is involved in transport of cholesterol. Inheritance of certain APOE gene variants is linked to risk for some cardiovascular disorders.[133] Testing for APOE variants is not a standard test in cardiology practice today, but it is used sometimes by cardiologists to help guide clinical decisions for their patients.[134]

In addition to indicating risk for some forms of cardiovascular disease, data indicate that inheritance of one particular APOE variant, APOE4, is linked to a higher incidence of late-onset Alzheimer disease in some populations.[135] The test's power to predict Alzheimer disease risk, however, is limited, and no established clinical preventive measures exist for those who test positive. While inheritance of one or two copies of the APOE4 variant is associated with increased risk for late-onset Alzheimer disease, many individuals with an APOE4 variant do not develop the disease, and a large percentage of

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[128] J. T. R. Wilcke, "Late-Onset Genetic Disease: Where Ignorance Is Bliss, Is It Folly to Inform Relatives?" *British Medical Journal* 317 (1998): 744.

[129] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 125. An additional 1 in 800 individuals has a genotype associated with a somewhat lower degree of risk.

[130] Wilcke, "Late-Onset Genetic Disease," 744.

[131] For discussion of gene polymorphism, see Chapter 1, page 12.

[132] Possible genotypes are E2/E2, E3/E3, E4/E4, E2/E3, E2/E4, E3/E4.

[133] P. W. F. Wilson et al., "Apolipoprotein E Alleles, Dyslipidemia, and Coronary Heart Disease: The Framingham Offspring Study," *Journal of the American Medical Association* 272 (1994): 1666.

[134] R. Wachbroit, "The Question Not Asked: The Challenge of Pleiotropic Genetic Tests," *Kennedy Institute of Ethics Journal* 8 (1998): 131, 133; H. T. Greely, "Special Issues in Genetic Testing for Alzheimer Disease," *Genetic Testing* 3 (1999): 115, 117–118. Greely reported results from a telephone survey of clinical laboratories in which three United States laboratories estimate performance of "hundreds" and in one case "thousands" of tests for this purpose annually.

[135] S. Seshadri, D. A. Drachman, and C. F. Lippa, "Apolipoprotein E4 Allele and the Lifetime Risk of Alzheimer's Disease: What Physicians Know, and What They Should Know," *Archives of Neurology* 52 (1995): 1074; Greely, "Special Issues in Genetic Testing for Alzheimer Disease."

individuals with Alzheimer disease lack the APOE4 variant.[136] Based on current information about the linkage between Alzheimer disease and the APOE4 gene variant, professional societies and consensus panels have agreed that APOE genetic testing should not be used for prediction of Alzheimer disease.[137]

### *Benefits and Risks of Late-Onset Testing*

#### Benefits of Testing

##### Reduced Morbidity and Mortality

For some genetic tests, a positive test result (confirming inheritance of a mutation) may enable individuals to adopt preventive interventions; these tests are said to have clinical utility.[138] For example, individuals with a susceptibility mutation for colorectal cancer can undergo frequent colonoscopy. Individuals who learn that they are susceptible to particular environmental agents can reduce their disease risk by avoiding exposure to those agents. For example, individuals who learn that they have inherited an alpha-1 antitrypsin deficiency and are at much higher risk than the general population for smoking-related disorders can greatly reduce their risks by avoiding cigarette smoking.

In cases of familial mutations, a negative test result can spare individuals the need to undergo often frequent and invasive monitoring, such as periodic colonoscopy. As an example of what one researcher refers to as a "best case" scenario for predictive genetic testing, a woman at very high risk for breast cancer based on family history was spared planned prophylactic mastectomy when testing results showed that she had not inherited the familial BRCA1 gene mutation.[139]

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[136] Individuals who inherit one APOE4 allele have a doubled risk for late-onset Alzheimer disease, but their lifetime risk is less than 30 percent. Seshadri, Drachman, and Lippa, "Apolipoprotein E4 Allele and the Lifetime Risk of Alzheimer's Disease," 1074. Risk is higher, but not 100 percent, for individuals who inherit two copies of APOE4, about 1 to 2 percent of the population. ACMG/ASHG, "Statement on Use of Apolipoprotein E Testing for Alzheimer Disease," *Journal of the American Medical Association* 274 (1995): 1627. See also Chapter 1, page 18.

[137] ACMG/ASHG, "Statement on Use of Apolipoprotein E Testing," 1627; National Institute on Aging/Alzheimer's Association Working Group, "Apolipoprotein E Genotyping in Alzheimer's Disease," *The Lancet* 347 (1996): 1091; S. G. Post et al., "The Clinical Introduction of Genetic Testing for Alzheimer Disease: An Ethical Perspective," *Journal of the American Medical Association* 277 (1997): 832; L. M. McConnell et al., "Genetic Testing and Alzheimer Disease: Has the Time Come?" *Nature Medicine* 4 (1998): 757.

[138] For discussion of clinical utility, see Chapter 2, page 43.

[139] F. S. Collins, "The Human Genome Project and the Future of Medicine," *Annals of the New York Academy of Sciences* 882 (1999): 42, 48; see also B. Ponder, "Genetic Testing for Cancer Risks," *Science* 278 (1997): 1050, 1051.

## *Psychological Benefits*

Reducing uncertainty is one of the most common reasons that individuals choose to undergo predictive genetic testing.[140] For some identified familial mutations, a negative test result can relieve anxiety about personal risk. In one study, for example, high-risk individuals who tested negative for a familial BRCA1 mutation showed statistically significant reduction in depressive symptoms.[141] Those who test positive for a mutation also may benefit psychologically from the reduction of uncertainty and the ability to make life-planning decisions, as was seen for many individuals who learned they were at risk for Huntington disease.[142] In another example, one woman who learned that she had inherited two copies of the APOE4 gene variant linked to Alzheimer disease risk stated that after initial "devastation," she was glad she had been tested and that the knowledge has provided more control in her life.[143]

### *Informed Reproductive Choices*

Testing may be used to inform reproductive decisions. Individuals who would refrain from reproduction — for example, those with a family history of Huntington disease — may choose differently when informed that they have not inherited the disease-associated mutation.[144] Individuals who test positive for a mutation may opt to use reproductive testing, including pre-implantation and prenatal testing, to allow for the birth of an unaffected child.[145]

### *Other Potential Benefits*

Additional benefits cited by some individuals who undergo testing are the ability to provide information about genetic risk to their offspring[146] and other family members and to contribute to scientific research.[147] In addition to directly benefiting individuals, negative genetic test results for individuals in affected families can save health care dollars otherwise spent in monitoring and/or intervention.[148] For example, within families affected by one

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[140] T. M. Marteau and R. T. Croyle, "The New Genetics: Psychological Responses to Genetic Testing," *British Medical Journal* 316 (1998): 693.

[141] C. Lerman et al., "BRCA-1 Testing in Families with Hereditary Breast-Ovarian Cancer: A Prospective Study of Patient Decision Making and Outcomes," *Journal of the American Medical Association* 275 (1996): 1885.

[142] See page 61, this chapter.

[143] L. Saslow, "Alzheimer's Gene Test: Facing the Answer," *New York Times*, May 3, 1998, Section 14, 19.

[144] See page 62, this chapter.

[145] See pages 51 and 53, this chapter.

[146] See, e.g., S. Loader, J. C. Levenkron, and P. T. Rowley, "Genetic Testing for Breast-Ovarian Cancer Susceptibility: A Regional Trial," *Genetic Testing* 2 (1998): 305.

[147] Saslow, "Alzheimer's Gene Test," 19.

[148] Unites States Department of Health and Human Services, "Health Insurance in the Age of Genetics," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/NEWS/Insurance*, visited January 26, 1999.

form of familial colon cancer, one study showed that health care costs were reduced by the use of genetic testing as compared to conventional clinical strategies.[149]

### *Risks of Testing*

#### *Limited Test Validity*

For susceptibility testing, limits to clinical validity, that is, limitations to the test's ability to predict who will or will not develop a gene-associated disorder, are of concern. The rush to market tests before clinical validity is sufficiently established for the general population poses the risk of unwarranted testing, unnecessary psychological distress, and harms associated with unnecessary or prematurely implemented medical treatment. Data collected from high-risk research subjects may not be representative of findings for other individuals, as was seen for BRCA testing.[150] Genetic test development based on research with population groups not representative of the general population also may miss disease-associated variants common in minority population groups, such as African Americans.[151]

Even for tests with established clinical validity, including presymptomatic tests, there is a chance of a general testing error, including sample mix-ups or reporting errors. In one example, two individuals who had inherited a mutation for Huntington disease underwent linkage testing and were told that they were not at risk, based on errors in assembling of family pedigree information.[152] In another example, a woman incorrectly informed that she had inherited a BRCA1 gene mutation that placed her at risk for breast and ovarian cancer had her ovaries removed before learning of the testing error.[153]

#### Limited Clinical Utility and Psychological Risks

The development of clinical interventions lags behind the ability to predict future disease. This lag has been referred to as a "therapeutic gap."[154] When a serious disease for which no interventions exist is predicted, psychological distress may result. This

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[149] B. Bapat et al., "Cost Comparison of Predictive Genetic Testing Versus Conventional Clinical Screening for Familial Adenomatous Polyposis," *Gut* 44 (1999): 698.

[150] N. A. Holzman et al., "Predictive Genetic Testing: From Basic Research to Clinical Practice," *Science* 278 (1997): 602.

[151] S. Lehrman, "Do You Really Want to Know Your Future?"

[152] E. Almqvist et al., "Risk Reversals in Predictive Testing for Huntington Disease," *American Journal of Human Genetics* 61 (1997): 945, 946–947. In the 1980s, two related individuals received incorrect interpretations of DNA linkage analysis tests. Both individuals were initially informed that they were not likely to have inherited the familial mutation and were later informed that they most likely had inherited the mutation.

[153] R. Weiss, "Genetic Testing's Human Toll," W*ashington Post*, July 21, 1999, A1.

[154] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 3.

scenario for Huntington disease testing, which can now predict familial risk with virtually 100 percent certainty, prompted one commentator to ask: "Do you want to know how and when you are going to die, especially if you have no power to change the outcome? Should such knowledge be made freely available? How does a person choose to learn this momentous information? How does one cope with the answer?"[155] A recent worldwide assessment of response to a positive predictive test result for Huntington disease showed that almost 1 percent of such cases resulted in a "catastrophic event" such as psychiatric hospitalization or a suicide attempt.[156]

Preventive interventions also may be limited or nonexistent for other, more common, disorders for which susceptibility testing is available, such as Alzheimer disease and cancer. In such cases, testing may cause psychological distress. A specialist on Alzheimer disease stated, "If we tell you what your [APOE type] is, the only thing we can do is potentially depress or elate you, with no substantive thing we can do as a result."[157] One cancer specialist stated that patients avoid testing because they fear living with the results, telling him, "I'm not sure I could handle it psychologically."[158] Some studies, however, show that receiving susceptibility test results (for example, for breast cancer risk) has little impact on anxiety or depression.[159] One study suggested that decisions not to test also might be harmful. [160] In this case, individuals in families known to carry BRCA gene mutations and who showed a high baseline for familial cancer-related stress experienced increased depressive symptoms after declining genetic susceptibility testing.

*Misinterpretation of and Misunderstanding Test Results*

The increased role of primary care physicians — who typically lack training in genetics — in ordering and interpreting susceptibility tests raises concerns that test results may not be interpreted correctly.[161] For example, one study showed that physicians sometimes misinterpreted the meaning of a negative test result for a mutation associated with familial colon cancer risk.[162] In this case, the DNA-based test used is insensitive to the detection of certain types of mutations,[163] but some physicians interpreted a negative test

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[155] N. S. Wexler, "The Tiresias Complex: Huntington's Disease as a Paradigm of Testing for Late-Onset Disorders," *FASEB Journal* 6 (1992): 2820.

[156] Almqvist et al., "Suicide, Suicide Attempts, or Psychiatric Hospitalization after Predictive Testing," 1293. Forty-four of 4,527 individuals showed a severe psychiatric response.

[157] L. Wingerson, *Unnatural Selection: The Promise and the Power of Human Genome Research* (New York: Bantam Books, 1998), 125 (quoting Dr. Allen Roses, Duke University).

[158] G. Kolata, "Genetic Testing Falls Short of Public Embrace," *New York Times*, March 27, 1998, A16 (quoting Dr. Henry Lynch of Creighton University, Omaha).

[159] Marteau and Croyle, "Psychological Responses."

[160] C. Lerman et al., "What You Don't Know Can Hurt You: Adverse Psychological Effects in Members of BRCA1-Linked and BRCA2-Linked Families Who Decline Genetic Testing," *Journal of Clinical Oncology* 16 (1998): 1650.

[161] For a discussion, see Chapter 12, page 362.

[162] F. M. Giardiello et al., "The Use and Interpretation of Commercial APC Gene Testing for Familial Adenomatous Polyposis," *New England Journal of Medicine* 336 (1997): 823.

[163] See Chapter 2, page 38.

result to rule out any chance of mutation. Such an error could result in the abandonment of surveillance measures by at-risk individuals, with potentially life-threatening consequences. Providers also may misunderstand the effectiveness of available interventions and the need to provide adequate posttest counseling. For example, prior to confirmation that prophylactic mastectomy significantly reduces breast cancer incidence in women at heightened risk due to family history, one survey showed that 28 percent of nonsurgeon physicians and 50 percent of surgeons would have recommended prophylactic mastectomy to women who test positive for a BRCA1 mutation.[164]

There also is a risk that individuals being tested will misunderstand correctly interpreted probabilistic test results. Evidence indicates that many people have an overly deterministic perception of genes and an inadequate understanding of probability.[165] This might result in unwarranted distress following a positive test result; it also might result in false reassurance that someone who tests negative for a susceptibility variant is at no risk for future disease.

*Potential of Discrimination*

One risk that influences testing decisions is the possibility that a positive test result may lead to the adverse use of genetic information in insurance or employment decisions.[166] Definitive data are lacking and are difficult to document, but most practitioners and professional organizations acknowledge that such concerns are well founded. The American Society for Clinical Oncology, in a 1996 statement regarding genetic testing for cancer susceptibility, acknowledged the potential for discrimination by health insurers.[167] A fact sheet issued by the National Human Genome Research Institute (NHGRI) states that fear of insurance discrimination has deterred some women from obtaining BRCA gene testing and that "their fears are not irrational."[168] Several clinical centers that offer BRCA testing reported that the most common reason cited to forgo testing are concerns about confidentiality, health insurance, and discrimination-related financial sequelae.[169]

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[164] G. Geller et al., "Decision-Making about Breast Cancer Susceptibility Testing: How Similar Are Attitudes of Physicians, Nurse Practitioners, and At-Risk Women?" *Journal of Clinical Oncology* 16 (1998): 2868. Subsequently, a 1999 published study established the clinical efficacy of prophylactic mastectomy for breast cancer prevention. See L. C. Hartmann et al., "Efficacy of Bilateral Prophylactic Mastectomy in Women with a Family History of Breast Cancer," *New England Journal of Medicine* 340 (1997): 77.

[165] See Chapter 4, page 91.

[166] For a discussion, see Chapter 10.

[167] American Society of Clinical Oncology, "Statement of the American Society of Clinical Oncology: Genetic Testing for Cancer Susceptibility," 1734–1735.

[168] National Human Genome Research Institute Office of Communications, *Fact Sheet: Genetic Discrimination in Health Insurance*, October 1997, website: *http://www.nhgri.nih.gov*, visited November 12, 1998.

[169] Mann and Borgen, "Breast Cancer Genes," 272; Department of Health and Human Services, "Health Insurance in the Age of Genetics;" M. K. Cho et al., "Commercialization of BRCA1/2 Testing: Practitioner Awareness and Use of a New Genetic Test," *American Journal of Medical Genetics* 83 (1999): 157.

A positive test result also may lead to social stigmatization. Stigmatization may be particularly likely for genetic variants that are associated with behavioral or psychological disorders.[170] Also, some have expressed concerns about stigmatization of ethnic or racial groups based on genetic research within defined subpopulations.[171] In the United States, for example, some commentators have expressed concern that research focusing on the Ashkenazi Jewish community is placing the community and its members at risk of stigmatization.[172] One member of the community asked, "All the bad genes you talk about are Jewish genes. Why?"[173]

*Perturbation of Family Relationships*

Genetic testing may perturb family relations, based on the sharing of gene variants (and associated risks) within families. Some members may seek genetic information, whereas others may not wish to know of the existence of a familial mutation, especially in the absence of an effective intervention. Faced with a positive predictive test result for a dominant disorder by a parent or sibling, an individual is confronted with a fifty-fifty chance that he or she is at similar risk.[174] A recent study of a large multigenerational family affected by both a BRCA1 and a BRCA2 gene mutation illustrated the different responses of family members to the knowledge of the familial mutations, different individual decisions about whether to test, and altered family perceptions as a result of testing.[175] Another study found that Huntington disease testing had significant impact on family structure and communication, including "loss of family membership" based on genetic testing decisions or results.[176]

Partners of individuals who are informed of an inherited risk for a late-onset disorder also may experience distress, and relationships may be perturbed.[177] Another potential risk is the inadvertent disclosure of the nature of family relationships, including misattributed paternity or undisclosed adoption.[178]

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[170] J. Beckwith and J. S. Alper, "Behavioral Genetics: Dangers of Stigmatization," *The Genetic Resource* 10, no. 1 (1996): 59.

[171] S. Lehrman, "Coalition to Pursue Ethnic Concerns over Gene Research," *Nature* 392 (1998), 428.

[172] S. G. Stohlberg, "Concern among Jews Is Heightened as Scientists Deepen Gene Studies," *New York Times*, April 22, 1998, A24; R. Weiss, "Discovery of 'Jewish' Cancer Gene Raises Fears of More Than Disease," *Washington Post*, September 3, 1997, A3.

[173] Stohlberg, "Concern among Jews Is Heightened" (quoting Rabbi Moshe David Tendler of Yeshiva University).

[174] For an identical twin, the risk is identical. Also, for late-onset disorders such as Huntington disease, a parent who does not wish to know whether he/she has inherited a familial mutation may learn that he/she has inherited it if their adolescent or adult child undergoes testing and tests positive.

[175] S. Loader and P. T. Rowley, "Deleterious Mutations of Both BRCA1 and BRCA2 in Siblings," *Genetic Testing* 2 (1998): 75, 77.

[176] S. K. Sobel and D. Brookes Cowan, "Impact of Genetic Testing for Huntington Disease on the Family System," *American Journal of Medical Genetics* 90 (2000): 49, 52–53.

[177] Ibid.; Marteau and Croyle, "Psychological Responses."

[178] See Chapter 4, page 100.

## Beyond Clinical Disease Prediction: Biomarkers

In addition to diagnostic testing and predictive testing to detect heritable health risks, researchers also are developing new applications for genetic testing to promote human health. These applications focus on inherited genetic variation that occurs in genes that code for proteins involved in the handling, activation, or neutralization of various drugs or environmental toxins. These variants are called genetic biomarkers (biological markers).[179] Currently, molecular epidemiological research is identifying biomarkers that provide information about potential beneficial and adverse effects of drugs in different individuals (pharmacogenetic biomarkers) and identify susceptibility to particular environmental agents (biomarkers of susceptibility).[180]

### Biomarkers for Treatment: Pharmacogenetics

Genetic variations among individuals influence both positive and adverse responses to new drugs. The study of these variations is called pharmacogenetics.[181] For example, one study showed that responsiveness to pravastatin, a drug designed to lower serum cholesterol levels and reduce heart attack risk, is linked to specific variations in a gene that specifies a protein called cholesterol ester transferase protein (CETP).[182] Variation in another gene that specifies a blood-clotting protein called factor V is another example of a gene variation for which DNA-based testing can identify a minority of individuals at increased risk for adverse effects of particular drugs. In this case, about 5 percent of Caucasian women possess a gene variant that makes them more susceptible to formation of potentially lethal blood clots, the risk for which is increased by taking certain oral contraceptives or hormonal treatments used to treat and prevent breast cancer.[183]

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[179] Office of Technology Assessment, *Genetic Monitoring and Screening in the Workplace* (Washington, D.C.: U.S. Government Printing Office, 1990), 5.

[180] Further in the future, DNA-based analysis also may lead to genetic testing for "biomarkers of exposure," acquired mutations that provide a "fingerprint" for a specific environmental exposure.

[181] P. W. Kleyn and E. S. Vesell, "Genetic Variation as a Guide to Drug Development," *Science* 281 (1998) 1820; "Designer Drugs," *British Medical Journal* (1998): 316; M. Maan, "Pharmacogenetics — Taking It Personally," *American Medical News*, October 5, 1998, 37; W. E. Evans and M. V. Relling, "Pharmocogenomics: Translating Functional Genomics into National Therapeutics," *Science* 286 (1999): 487; A. D. Roses, "Pharmacogenetics and the Practice of Medicine," *Nature* 405 (2000): 857.

[182] J. A. Kuivenhoven et al., "The Role of a Common Variant of the Cholesterol Ester Transfer Protein Gene in the Progression of Coronary Athlerosclerosis," *New England Journal of Medicine* 338 (1998): 86.

[183] S. F. T. M. de Bruijn et al., "Case-Control Study of Risk of Cerebral Sinus Thrombosis in Oral Contraceptive Users Who Are Carriers of Hereditary Prothrombotic Conditions," *British Medical Journal* 316 (1998): 589; I. C. Weitz, V. K. Isreal, and H. A. Liebman, "Tamoxifen-Associated Venous Thrombosis and Activated Protein C Resistance Due to Factor V Leiden," *Cancer* 79 (1997): 2024.

Pharmaceutical companies are using genomic approaches to obtain information about gene variants that underlie individual responses to drug treatments.[184] This approach, called pharmacogenomics, could enable drug companies to target their clinical trials to subpopulations that are likely to respond with more positive and/or fewer adverse effects. For physicians and patients, genetic testing to tailor treatments for individual patients could enable faster and safer treatment protocols. Pharmacogenomics also will likely lead to development of targeted DNA-based drug therapies.

Many predict that pharmacogenetics will lead the way to individualized medicine and enter mainstream clinical care in the next several years.[185] Generally, clinicians will offer pharmacogenetic testing for a clear medical benefit. However, some have expressed concerns about potential risks based on possible misuse of genetic profile data in an individual's medical record and on the possibility that pharmaceutical companies may direct their pharmacogenetic research and development toward specific classes of people.[186]

**Biomarkers of Susceptibility to Environmental Agents**

Biomarkers of environmental susceptibility are genetic variants that confer susceptibility to adverse effects of particular environmental exposures.[187] For example, inheritance of variant forms of a set of related genes called P450 influences metabolism of many environmental chemicals, including steroids and pollutants. About 10 percent of Caucasians have a particular P450 gene variant that significantly increases cancer risks associated with cigarette smoking.[188]

A potential focus of biomarker susceptibility testing is workplace screening of employees to detect individuals at increased genetic risk for specific exposure-related disorders.[189] For example, workplace exposure to chemicals called aromatic amines is associated with bladder cancer; individuals with a specific variant of a gene called N-acetyltransferase are at increased risk.[190]

While few, if any, companies currently screen for biomarkers of susceptibility,[191] this may change. Researchers currently are seeking a genetic biomarker to screen 10,000

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[184] L. M. Fisher, "Smoother Road from Lab to Sales: DNA Technique Aims to Predict Whom a Drug Will Benefit," *New York Times*, February 25, 1998, D1–D5.

[185] Roses, "Pharmacogenetics and the Practice of Medicine," 858; see also G. Kolata, "Using Gene Tests to Customize Medical Treatments," *New York Times*, December 20, 1999, A1; R. Weiss, "The Promise of Precision Prescriptions," *Washington Post*, June 23, 2000, A01.

[186] Weiss, "The Promise of Precision Prescriptions."

[187] Office of Technology Assessment, *Genetic Monitoring*, 5. In the absence of a specific environmental exposure, these biomarkers would not place an individual at any health risk.

[188] F. P. Perera, "Environment and Cancer: Who Are Susceptible?" *Science* 278 (1997): 1068, 1070.

[189] Office of Technology Assessment, *Genetic Monitoring*, 5.

[190] P. W. Brandt-Rauf and S. I. Brandt-Rauf, "Biomarkers — Scientific Advances and Societal Implications," in *Genetic Secrets*, 187.

[191] American Management Association, *1999 AMA Survey on Workplace Testing: Medical Testing*. The survey of 1,054 major United States firms reported that a small number of firms have employee genetic

workers exposed to the metal beryllium to identify a minority who may be susceptible to development of an incurable lung disease.[192] Also, the National Institutes of Environmental Health and Sciences has launched the Environmental Genome Project, a multidisciplinary and collaborative project that aims to document the variation of human genes that affect responses to environmental exposures.[193]

## *Issues Surrounding Pleiotropic Genetic Information*

A single gene may affect multiple, seemingly unrelated traits; this is referred to as pleiotropy.[194] Inheritance of a mutant variant of such a gene may affect risk for seemingly unrelated health conditions. As a result of pleiotropy, individuals undergoing testing to assess a risk for a particular disease or condition (or for pharmacogenetic reasons)[195] may inadvertently learn that they also are at increased risk for an unrelated condition. Concerns raised by one health condition may vary considerably from those for another condition.[196] Genetic risk information for different health conditions learned from a single test also may have different levels of clinical predictive value and utility (including availability of preventive or therapeutic interventions) for the different conditions.

One commentator has referred to genetic testing that provides risk information about unrelated health conditions as pleiotropic genetic testing;[197] another has referred to it as "versatile" testing.[198] An example is genetic testing of the APOE gene to determine which (and how many copies) of each of three major gene variants (APOE2, APOE3, and APOE4) an individual has inherited.[199] Thousands of persons have undergone testing to determine their APOE variant status as part of research or commercial testing based on a complex association of APOE status with cardiovascular disease risk.[200] Genetic

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testing programs, e.g., for "breast and colon cancer." Twelve percent of firms responded that they perform employee testing for susceptibility to workplace testing, not specified as genetic testing.

[192] E. Marshall, "Beryllium Screening Raises Ethical Issues," *Science* 285 (1999): 178.

[193] See National Institutes of Environmental Health and Safety website: *http://www.niehs.nih.gov/envgenom*, visited August 3, 2000; see also M. Wadman, "Genome Study Maps Chemical Sensitivity," *Nature* 389 (1997): 774; "New HGP Spinoff Program to Study Genes for Environmental Risk," *Human Genome News* 9 (1998): 10. For a discussion of polymorphism, see Chapter 1, page 12.

[194] See Chapter 1, page 14.

[195] See Chapter 2, page 74.

[196] Wachbroit, "The Question Not Asked," 132.

[197] Ibid., 131.

[198] Juengst, "Caught in the Middle Again," 196.

[199] See page 67, this chapter.

[200] See Greely, "Special Issues in Genetic Testing for Alzheimer Disease," 117–118; see also Chapter 7, page 193.

information about one's APOE status, however, also may provide risk information for late-onset Alzheimer disease, for which no established preventive measures exist.[201]

As more associations between disorders and gene variants are discovered, the incidence of pleiotropic test information is likely to increase. The degree of relatedness of conditions may vary. Some disorders affecting cardiac disease risk also may affect conditions that have significant comorbidity with cardiac disease, such as obesity and diabetes.[202] Gene mutations that increase risk for one type of cancer also may increase risk for other types of cancer or for unrelated diseases. For example, one research study showed that a gene mutation that increased tumor incidence in an experimental mouse model also resulted in an increase in lupus-like autoimmunity.[203]

Knowledge about pleiotropic effects of particular gene variants may be known at the time of development of a genetic test or may only become apparent months or years later. For example, from the initial offering of BRCA gene testing, inheritance of particular BRCA gene mutations was known to increase risk for both breast and ovarian cancer.[204] Several years later, however, research showed that inheritance of a BRCA2 mutation may also significantly increase risk for other types of cancer, including prostate cancer in men.[205] This pleiotropic character of genetic testing raises special concerns for informed consent and counseling and for the psychosocial risks associated with predictive testing.[206]

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[201] Wachbroit, "The Question Not Asked," 133; see also O. Kosunen et al., "Relation of Coronary Athlerosclerosis and Apolipoprotein E Genotypes in Alzheimer Patients," *Stroke* 26 (1995): 743.

[202] See "Getting to the Heart of the Matter," *Nature Genetics* 19 (1998): 12; "Leptin and Heart Disease," *Journal of the American Medical Association* 280 (1998): 125.

[203] A. Di Cristofano et al., "Impaired Fas Response and Autoimmunity in Pten+/– Mice," *Science* 285 (1999): 2122.

[204] See page 63, this chapter.

[205] The Breast Cancer Linkage Consortium, "Cancer Risks in BRCA2 Mutation Carriers," *Journal of the National Cancer Institute* 91 (1999): 1310.

[206] See Chapter 7, page 193.

# 4

# Social Perceptions, Misperceptions, and Misuses of Genetics

For centuries, people have believed that heredity can influence and even determine a person's behavioral as well as physical traits. Examples include Shakespeare's "blood-as-fate" references and cultural lore of "bad blood" and "bad seeds."[207] From the late 1800s through the twentieth century, science generated theories and evidence about how heredity works. From Darwin's theory of evolution by natural selection and Mendel's genetic laws, subsequent scientific discoveries throughout the past century have influenced how people view the power of heredity and have contributed to a continuous "nature-nurture" debate. This debate attempts to determine the relative roles of hereditary (nature) versus environmental (nurture) influences on individuals — their health, their behaviors, and their fates.

Relative emphasis on the role of nature and of nurture has shifted during different periods and in different contexts throughout the past century. For example, a nurture-biased emphasis on the role of family and social factors in influencing personal fate prevailed in criminology in the 1950s.[208] The role of nature, however, has been emphasized during much of the last century, attributing a central role of inborn traits to personal behaviors and fates, leading to what some have called genetic determinism. Genetic determinism is a belief that genes predetermine individuals' fates and that genetic inheritance is immutable.[209] Within the United States and parts of Europe, genetic determinism was especially strong during the first third of the twentieth century. The era's enthusiasm for the new science of genetics was sometimes translated, misguidedly, into social policy. One manifestation was social eugenic programs to promote "good births" and discourage "bad births." [210]

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[207] D. Nelkin and S. M. Lindee, *The DNA Mystique: The Gene as a Cultural Icon* (New York: W. H. Freeman and Company, 1995), 15; J. Osber, "Gene Blues," *Salon Magazine* (April 1998), website: *http://www.salonmagazine.com*, visited April 8, 1998.

[208] Nelkin and Lindee, *The DNA Mystique*, 33–34; D. C. Wertz, "Society and the Not-So-New Genetics: What Are We Afraid Of? Some Predictions from a Social Scientist," *Journal of Contemporary Health Law and Policy* 13 (1997): 299, 307; R. Hubbard and E. Wald, *Exploding the Gene Myth*, 3d ed. (Boston: Beacon Press, 1999). The authors claim that, in the United States, "nurture" prevailed during the Great Depression of the 1930s and again following World War II through the 1960s, until momentum shifted back to "nature" during the early 1970s. For a discussion of shifting perspectives about nature versus nurture and criminality, see page 85, this chapter.

[209] For a discussion of biological and genetic determinism, see Hubbard and Wald, *Exploding the Gene Myth*, 3.

[210] See page 80, this chapter.

In the midst of the current genetics "information revolution,"[211] some commentators see a renewed tendency to overemphasize hereditary, as opposed to environmental, influences on health, behavioral, and cognitive factors.[212] Past eugenic practices and other reflections of genetic determinism raise concerns as the Human Genome Project promotes genomic research and medicine. This chapter frames and examines some of these concerns.

## Genetics in the Twentieth Century: Misperceptions and Misuses

### Eugenics

#### *What Is Eugenics?*

The word "eugenics" derives from the Greek *eugenes*, which means good or noble birth. The term was introduced in 1883 by Francis Galton, a scientist and cousin of Charles Darwin, as "the science of improvement of the human race germ plasm through better breeding."[213] The goal of eugenics was to produce a "highly gifted race of men" within several generations.[214] Over the next several decades, two approaches were used in attempts to attain this goal. "Positive eugenics" sought to promote reproduction by "fit" individuals and classes, while "negative eugenics" discouraged or prevented births among the "unfit" or "defective." Although some define eugenics broadly to include any reproductive decision to promote a healthy birth, the term generally has come to refer to a systematic and sometimes coercive social policy of birth promotion or prevention.[215]

Eugenic concepts predate the science of genetics, indeed of Western science generally. In fact, advocacy of a eugenic social policy can be found as early as Plato's

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[211] E. S. Lander, "Scientific Commentary: The Scientific Foundations and Medical and Social Prospects of the Human Genome Project," *Journal of Law, Medicine, and Ethics* 26 (1998): 184.

[212] Nelkin and Lindee, *The DNA Mystique*; Hubbard and Wald, *Exploding the Gene Myth*. Some commentators, however, disagree with the view that genetic determinism in mass culture has increased in recent decades, arguing that it is unchanged or, by some indicators, decreasing. See C. M. Condit, N. Ofulue, and K. M. Sheedy, "Determinism and Mass-Media Portrayals of Genetics," *American Journal of Human Genetics* 62 (1998): 979.

[213] Board of Directors of the American Society of Human Genetics, "Eugenics and the Misuse of Genetic Information to Restrict Reproductive Freedom," October 1998, American Society of Human Genetics website: *http://www.faseb.org/genetics/policy/pol-30.htm*, visited February 24, 1999.

[214] D. J. Kevles, *In the Name of Eugenics*: *Genetics and the Uses of Human Heredity* (Cambridge, MA: Harvard University Press, 1995), 4, 46, 74. Galton equated "racial" identity with national identity, e.g., distinguishing among Anglo Saxons, Poles, Irish, and Italians.

[215] D. C. Wertz, " Eugenics Is Alive and Well: A Survey of Genetics Professionals," *Science in Context* 11 (1998): 493; D. C. Wertz, "Eugenics: Definitions," *The Gene Letter* (February 1999), website: *http://www.geneletter.org*, visited May 4, 1999; see also A. L. Kaplan, G. McGee, and D. Magnus, "What Is Immoral about Genetics?" *British Medical Journal* 319 (1999): 1284.

*Republic*.[216] Plato, who believed that temperament is inherited, envisioned an ideal society in which men who showed exceptional courage in battle would be given extra opportunities to father as many sons as possible. A negative eugenic practice, the abandonment of unwanted infants, occurred throughout the ancient Western world (and elsewhere); in Europe, it persisted up to the Industrial Revolution.[217]

Misapplication of the new scientific ideas of the late 1800s and early 1900s, however, was used to promote eugenic theories that supported existing stereotypes, prejudices, and class structures.[218] Galton's concept of eugenics derived from a flawed application of Darwin's theories and the concept of "survival of the fittest." Darwin's theory holds that members of a species that best "fit" a particular environment will be more likely to survive and to reach reproductive age than other species members that are "less fit" for that environment. For example, a gray butterfly that blends with an environment of gray twigs would be more likely than a black butterfly to escape predators and live long enough to reproduce.[219] The black butterfly, however, would have the adaptive survival (and, thereby, reproductive) advantage in an environment of black twigs. Neither butterfly is intrinsically superior to the other.

Galton mistakenly interpreted "fitness" in humans on an absolute scale (i.e., some humans are inherently superior to others) rather than on a relative scale (i.e., different individuals are more or less suited to different environments). Eugenic criteria for human "unfitness" included "immoral behavior," poverty, lower than average intelligence, and late-onset disorders such as Huntington disease, all of which generally do not influence the ability to reproduce.[220] In this skewed eugenic view, state-sponsored public health and social welfare programs that supported lower social classes were perceived as "artificial selection" that diverted the natural selection process and threatened race "degradation."[221]

## *Eugenic Policies in the United States*

The eugenics movement blossomed in the United States and England during the early 1900s. Known as the Progressive Era, this period was shaped by great enthusiasm that new technologies and medical and statistical sciences would help manage, and eventually cure, both social and medical ills.[222] From 1905 to 1910, eugenics was the

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[216] D. J. Galton, "Greek Theories in Eugenics," *Journal of Medical Ethics* 24 (1998): 263, 264; "A Brief History of Eugenics: Prologue," in *The Gene Letter* (February 1999), website: *http://www.geneletter.org*, visited May 4, 1999.
[217] "A Brief History of Eugenics."
[218] Nelkin and Lindee, *The DNA Mystique*, 16; see also M. Ridley, *Genome — The Autobiography of a Species in 23 Chapters* (New York: Harper Collins Publishers, 1999), 286–300.
[219] This example is provided by the authors of "A Brief History of Eugenics."
[220] Ibid.
[221] Kevles, *In the Name of Eugenics*, 70.
[222] Ibid., 72; M. S. Pernick, "Eugenics and Public Health in American History," *American Journal of Public Health* 87 (1997): 1767, 1768–1770; H. Markel, "The Stigma of Disease: Implications of Genetic Screening," *American Journal of Medicine* 93 (1992): 209, 211.

second most popular topic in American general circulation magazines[223] and was described by some as a "civic religion."[224] A 1928 survey of 499 American colleges and universities found that 343 offered courses in genetics and eugenics.[225] As one commentator remarks, to be against eugenics in this period was perceived to be "against modernity, progress, and science."[226] Eugenics was embraced by many prominent Americans, including President Theodore Roosevelt, who was concerned that immigration into the United States by groups other than Anglo-Saxons would lead to "race suicide."[227]

Positive eugenic activities included a nationwide system of contests promoting "better babies," "perfect schoolchildren," and "fitter families" based on physical measurements and performance criteria.[228] Negative eugenics also flourished and eventually included marriage and immigration restrictions, involuntary sterilization, and custodial commitment. A central focus for these activities was the Eugenics Record Office at Cold Spring Harbor, New York, established in 1904.[229] The director of the Eugenics Record Office, Charles Davenport, enthusiastically attempted to apply his understanding of Mendel's observations with pea plants[230] to human social problems. Davenport attributed behaviors such as lust, criminality, alcoholism, "pauperism," and "feeblemindedness" to genetic factors and believed that unfit genes were especially prevalent among particular ethnic groups.[231]

Between 1911 and 1924, Davenport's program trained and directed over 250 workers for field research in human genetics. Workers conducted genealogical surveys of families marked by often complex and ill-defined behaviors. Davenport analyzed and grossly oversimplified the collected data.[232] One commentator described his methods and approaches as "faulty compendiums of pedigree analyses and case studies based almost exclusively on subjective impressionistic data."[233]

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[223] P. R. Reilly, "A Look Back at Eugenics," *The Gene Letter* (November 1996), website: *http://www.geneletter.org*, visited January 29, 1998.
[224] Nelkin and Lindee, *The DNA Mystique*, 20, 30.
[225] Ibid., 21.
[226] L. Wingerson, *Unnatural Selection: The Promise and the Power of Human Gene Research* (New York: Bantam Books, 1997), 137 (quoting anthropologist Jonathan Marks).
[227] Kevles, *In the Name of Eugenics*, 74.
[228] Nelkin and Lindee, *The DNA Mystique*, 27–29.
[229] Kevles, *In the Name of Eugenics*, 45; see also the *Image Archive of the American Eugenics Movement*, Cold Spring Harbor Laboratory DNA Learning Center website: *http://vector.cshl.org/eugenics*, visited February 16, 2000.
[230] See Chapter 1, page 12.
[231] Kevles, *In the Name of Eugenics*, 46; Markel, "The Stigma of Disease," 211–212; Wingerson, *Unnatural Selection*, 140. Feeblemindedness was an ill-defined term that referred to a range of mental deficiencies and deviant behaviors.
[232] Kevles, *In the Name of Eugenics*, 48, 199.
[233] Markel, "The Stigma of Disease," 212.

The Eugenics Record Office also lobbied to promote restrictive immigration legislation. Testifying in a congressional hearing to support what would become the Immigration Restriction Act of 1924, Davenport's chief assistant, Harry H. Laughlin, stated that "recent immigrants (e.g., Russian and Polish Jews, Italians and Central Europeans), as a whole, present a higher percentage of inborn socially inadequate qualities (e.g., insanity, feeblemindedness, dependency, criminal behavior, deformities, tuberculosis, etc.) than do the older stocks (e.g., Nordics, Anglo Saxons, etc.)."[234] The immigration act implemented strict quotas aimed at preserving the status quo; the law remained in place until 1968.[235]

The eugenics movement also promoted passage of state laws that restricted or invalidated marriages or legalized involuntary sterilization.[236] Many states passed antimiscegenation laws prohibiting marriage between Caucasians and persons with as little as 1/16 non-Caucasian ancestry.[237] By 1914, about thirty states had enacted marriage laws declaring voidable the marriage of "idiots," the "insane," "habitual drunkards," and persons having a "transmissible disease."[238]

A similar number of states passed involuntary sterilization laws targeted at the mentally ill, the "feebleminded," and habitual or confirmed criminals.[239] Between 1907 and 1960, at least 60,000 such sterilizations were performed in the United States.[240] Although both males and females were subject to involuntary sterilization, most were performed on young women for whom the evidence of mental retardation was questionable or nonexistent.[241] One infamous case, involving the sterilization of seventeen-year-old Carrie Buck, culminated in the United States Supreme Court's 1927 *Buck v. Bell* decision,[242] in which Justice Oliver Wendell Holmes, upholding Virginia's sterilization statute, declared that "three generations of imbeciles are enough."[243] In this case, the Eugenics Record Office weighed in with its opinion that Buck, a domestic servant committed to a Virginia institution following the birth of an illegitimate child, displayed hereditary "feeblemindedness."[244]

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[234] Ibid., 210.

[235] P. R. Reilly and D. C. Wertz, "Eugenics: 1883–1970," *The Gene Letter* (February 1999), website: *http://www.geneletter.org*, visited May 4, 1999.

[236] Ibid.; Kelves, *In the Name of Eugenics*, 100.

[237] Wertz, "Eugenics Definitions." The laws were declared unconstitutional in 1967. *Loving v. Virginia*, 388 U.S. 1, 2, 87 S. Ct. 1817, 1818 (1967); see page 93, this chapter.

[238] Kevles, *In the Name of Eugenics*, 99–100.

[239] Ibid., 100–101; Reilly and Wertz, "Eugenics: 1883–1970"; see also N. A. Holtzman and M. A. Rothstein, "Eugenics and Genetic Discrimination," *American Journal of Human Genetics* 50 (1992): 457.

[240] Reilly and Wertz, "Eugenics: 1883–1970." Both men and women were sterilized. See also B. Baskerville, "Eugenics Is Gone, but Emotional Scars Still Linger," Nando Times website: *http://www.nando.com*, visited March 20, 2000. Sterilization of males was motivated not only to prevent reproduction; in some cases it was mistakenly intended to prevent "sexual overexcitation." Kevles, *In the Name of Eugenics*, 108.

[241] Reilly and Wertz, "Eugenics: 1883–1970."

[242] *Buck v. Bell*, 274 U.S. 200, 47 S. Ct. 584 (1927).

[243] *Ibid.*, 274 U.S. at 207, 47 S. Ct. at 585.

[244] Kevles, *In the Name of Eugenics*, 110–111. The Eugenics Record Office, without ever personally examining Buck or her relatives, declared the Bucks to be "shiftless, ignorant, and worthless class of anti-social whites of the south." See also M. A. Rothstein, "Behavioral Genetic Determinism: Its Effect on

The eugenics movement subsided in the United States after 1935 because of increasing challenges by secular and religious commentators, including many prominent scientists,[245] as well as reactions against the extreme racial policies adopted by Nazi Germany.[246] In 1935, geneticist and future Nobel laureate Herman J. Muller commented that eugenics had become "hopelessly perverted" into a pseudoscientific facade for "advocates of race and class prejudice, defenders of vested interests of church and state, Fascists, Hitlerites, and reactionaries generally."[247] The same year, a blue ribbon committee of scientists established to review Eugenics Record Office activities concluded that the office's records were "unsatisfactory for the study of human genetics." The office was shut in 1940.[248]

### *Eugenic Policies in Other Countries*

From the early 1900s, the American eugenics movement was linked to a strong social and academic eugenics movement in England, the home of Francis Galton.[249] Unlike the United States, however, England never passed eugenic legislation.[250] Other countries, including Canada and Sweden, influenced by American state sterilization policies and by other factors, instituted eugenic sterilization programs.[251] The best known and most extreme such policy was, of course, in Nazi Germany.[252] In 1934, Germany passed its racial hygiene law, which in the first year of its implementation led to the sterilization of about 80,000 persons without their consent.[253] The law created a system of "hereditary health courts" designed to hear and process petitions for sterilization. The program aimed to eliminate society's "useless eaters," including the mentally retarded and mentally ill; it also targeted individuals with, or at-risk for, certain hereditary diseases, including Huntington disease.[254] The program was originally independent of the

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Culture and Law," in *Behavioral Genetics — The Clash of Culture and Biology*, ed. R. A. Carson and M. A. Rothstein (Baltimore: Johns Hopkins University Press, 1999), 89, 98–99.

[245] Kevles, *In the Name of Eugenics*, 127–147. Many prominent American and British scientists, including those in the evolving field of genetics, were vocal critics throughout the eugenics movement.

[246] Ibid., 118–124, 164; Reilly, "A Look Back at Eugenics."

[247] Kevles, *In the Name of Eugenics*, 164. Muller had been a vocal proponent of positive eugenic activities. Ibid., 64; Wingerson, *Unnatural Selection*, 147.

[248] Kevles, *In the Name of Eugenics*, 199.

[249] Ibid., 37–40, 62–64.

[250] Ibid., 100–101, 104–106; see also Ridley, *Genome*, 286–297.

[251] Reilly and Wertz, "Eugenics: 1883–1970."

[252] For a discussion of eugenic practices in Nazi Germany, see Kevles, *In the Name of Eugenics*, 116–118; Wingerson, *Unnatural Selection*, 150–177; American Society of Human Genetics, "Eugenics and the Misuse of Genetic Information."

[253] Kevles, *In the Name of Eugenics*, 116. The German law was compulsory with respect to all persons, not just institutionalized persons, who suffered from a range of allegedly hereditary conditions, including feeblemindedness, blindness, epilepsy, and severe drug or alcohol addiction.

[254] Ibid.

regime's anti-Semitic policies, but, eventually, its sterilization and racist policies merged. In 1939, the government expanded its euthanasia policies to include more general classes, including all Jews.[255]

After World War II, Japan passed a Eugenic Protection Law that allowed for involuntary sterilization.[256] The law targeted up to fourth degree relatives of persons who had one of about a dozen specified, and presumed hereditary, conditions. There is no clear evidence that the law was enforced, and it was substantively amended in 1996 to remove all coercive overtones and the list of disorders.

**The Nature-Nurture Debate**

Some proponents of the mainstream eugenics movements in the United States and England used slipshod scientific data to promote overly deterministic views about inheritance of behavioral traits. Despite contrary views of many leading biologists, some eugenicists considered "behavioral failings" such as criminality or feeblemindedness to be highly heritable "unit characters," equivalent to the single-gene traits of Mendel's pea plants.[257]

One example of how slipshod interpretations of science, combined with media attention, promoted a gross overemphasis on the hereditary component of behavior is the century-long nature-nurture discourse on criminal behavior. In 1911, Italian criminologist Cesare Lombroso published research based on autopsies of criminals that claimed that the "criminal type" was associated with certain inherited physical characteristics.[258] The theory claimed that males possessing particular physical traits, including a low slanting forehead and a large jaw, were more likely to display criminal behavior. Others took up the theme. For example, in 1939, a Harvard anthropologist stated, "It is from the physically inferior element of the population that native born criminals of native parents are mainly derived."[259]

Throughout the 1950s and into the 1960s, sociological theories prevailed over biological ones, acknowledging the importance of social and other environmental factors in criminal behavior.[260] However, in 1965, a genetic testing study performed on inmates of a Scottish prison led to a revival of notions of genetic determinism. A researcher reported that the prison population had an unusually high frequency of males with an extra Y chromosome and that possession of two Y chromosomes was associated with a

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[255] Ibid., 115–116.
[256] D. C. Wertz, "State-Coerced Eugenics in the Postmodern World," *The Gene Letter* (February 1999), website: *http://www.geneletter.org*, visited June 7, 1999.
[257] Markel, "The Stigma of Disease," 212; Kelves, *In the Name of Eugenics*, 145–146.
[258] See S. Horan, "The XYY Supermale and the Criminal Justice System: A Square Peg in a Round Hole," *Loyola of Los Angeles Law Review* 25 (1992): 1343.
[259] Reilly, "A Look Back at Genetics" (quoting Professor E. A. Hooton).
[260] Nelkin and Lindee, *The DNA Mystique*, 134.

personality disorder that included "unusually aggressive behavior."[261] Through the next decade, others researchers and the media espoused the theory of the "criminal chromosome."[262] Later analyses identified study biases and led to dismissal of the "criminal chromosome" theory.[263]

## *Genetics in the Twenty-First Century*

### Human Behavioral Genetics
### *Role of Genes in Behavior and Cognition*

Scientific evidence shows that genes may influence complex behavioral and cognitive (intelligence) traits and mental illnesses.[264] Similar to most medical traits and disorders, however, behavioral and cognitive traits and disorders generally are determined by complex interactions of multiple genes and environmental factors, including prenatal, postnatal, biochemical, and social factors.[265] Even for the most well-defined mental illnesses that show familial inheritance patterns, such as bipolar disorder (also called manic depressive illness) and schizophrenia, the genetics of inheritance appears to be far more complex than the genetics of single-gene disorders such as Tay-Sachs disease and Huntington disease.[266] While individuals with a parent with schizophrenia are at greater risk to develop schizophrenia than the general population,[267] environmental factors also

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[261] P. A. Jacobs et al., "Aggressive Behavior, Mental Subnormality and XYY Male," *Nature* 208 (1965): 1351; Horan, "The XYY Supermale," 1347–1350. Normal males have one X and one Y chromosome. Males with an additional Y (referred to as an XYY phenotype) reportedly account for about 1 in every 1,000 male newborns. The 1965 study occurred before the general population incidence of the XYY phenotype was determined. In the prison population, 8 of 197 males tested (about 3.5 percent) had the XYY phenotype.

[262] Reilly, "A Look Back at Genetics."

[263] See Horan, "The XYY Supermale," 1349.

[264] S. Sherman et al., "Behavioral Genetics '97: ASHG Statement — Recent Developments in Human Behavioral Genetics: Past Accomplishments and Future Directions," *American Journal of Human Genetics* 60 (1997): 1265; R. Plomin, "Genetics and General Cognitive Ability," *Nature* 402 suppl. (1999): C25; R. Plomin and J. C. DeFries, "The Genetics of Cognitive Abilities and Disabilities," *Scientific American* (May 1998), 62; M. J. Owen and A. G. Cardno, "Psychiatric Genetics: Progress, Problems, and Potential," *The Lancet* 354 suppl. I (1999): 11; W. H. Berrettini, "Genetics of Psychiatric Disease," *Annual Review of Medicine* 51 (2000): 465.

[265] See Hubbard and Wald, *Exploding the Gene Myth*, 9–10; see also Chapter 1, page 17.

[266] J. Beckwith and J. S. Alper, "Human Behavioral Genetics: Dangers of Stigmatization," *The Genetic Resource* 11, no. 1 (1997): 5.

[267] For example, in one study, the prevalence of schizophrenia-related disorders in adopted children with an affected biological first-degree relative was 23.5 percent, versus 4.7 percent for adopted children without an affected biological relative (the general population rate is 1 to 2 percent). See Sherman et al., "Recent Developments in Human Behavioral Genetics," 1268.

influence development.[268] Also, for these familial disorders, the particular gene variants involved are likely to vary among different families.[269]

For general behavioral traits or dispositions, the complexity is even greater. Behavioral traits, such as aggressiveness and sociability, and cognitive traits, such as memory and reading ability, occur over a continuous scale. Genetically, any single gene's influence generally will be minor. For a given trait, many genes contribute probabilistically to account for individual differences along a continuous scale of normal variation.[270] The impact of environmental factors (e.g., the degree of mental stimulation received by an infant or preschool child) adds an additional level of complexity.

In addition to this intrinsic complexity, assessment criteria also vary and may be subjective because of the continuous scale of trait variations. In fact, many traits or behaviors, including criminal behavior, intelligence, sexual orientation, and alcoholism, are socially influenced constructs.[271] For example, one commentator points out that western Judeo-Christian views about human sexuality and sexual orientation differ from those of other cultures and affect concepts about "normal" behaviors.[272] For some traits, such as aggressiveness, concepts of normal and abnormal behaviors differ not only among cultures but also for a given culture, for different situations and environments.[273] Research to determine genetic components of some behaviors, such as addictive or violent behaviors, also sparks controversy because of the potential misuse of such work to justify discriminatory social policies.[274]

Despite these complexities, behavioral scientists have attempted to define genetic influences on behavioral and cognitive traits. For many decades, researchers have used family studies to try to distinguish genetic from environmental influences on behavior and intelligence traits. These studies include twin studies — for example, comparing identical twins who are raised together to those separated soon after birth and raised in different families.[275] In recent years, family study approaches have been coupled with

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[268] See Owen and Cardno, "Psychiatric Genetics," 11.

[269] Beckwith and Alper, "Human Behavioral Genetics," 6–7. For discussion of genetic heterogeneity, see Chapter 1, page 14. For a discussion of genetics and schizophrenia, see K. F. Schaffner, "Complexity and Research Strategies in Behavioral Genetics," in *Behavioral Genetics — The Clash of Culture and Biology*, 61, 64–67.

[270] Plomin, "Genetics and General Cognitive Ability," C27.

[271] Beckwith and Alper, "Human Behavioral Genetics," 5, 7; Hubbard and Wald, *Exploding the Gene Myth*, 93.

[272] P. R. Wolpe, "If I Am Only My Genes, What Am I? Genetic Essentialism and the Jewish Response," *Kennedy Institute of Ethics Journal* 7 (1997): 213, 215.

[273] See Hubbard and Wald, *Exploding the Gene Myth*, 105.

[274] See Beckwith and Alper, "Human Behavioral Genetics," 5; Parens, "Taking Behavioral Genetics Seriously," *Hastings Center Report* 13, no. 4 (1996): 15–16; Nelkin and Lindee, *The DNA Mystique*, 144–145; Sherman et al., "Recent Developments in Human Behavioral Genetics," 1265; D. Nelkin, "Biology Is Not Destiny," *New York Times*, September 28, 1995, A27.

[275] Sherman et al., "Recent Developments in Human Behavioral Genetics," 1266–1268; Plomin and DeFries, "The Genetics of Cognitive Abilities and Disabilities," 64. For discussion of the history of twin

new analytical techniques.[276] While promising, some have criticized these methods,[277] which are subject to limitations and cannot by themselves identify genes for further study. Newer molecular genetic technologies, however, may allow identification of specific gene variants that influence behaviors and cognitive abilities and contribute to mental disorders.

### *Molecular Genetics Research*

#### *Gene-Mapping Studies*

Molecular approaches include gene-mapping studies, which attempt to link chromosomal regions, and eventually specific gene variants, to specific traits or disorders.[278] This approach has successfully identified over 100 genes associated with single-gene disorders, such as cystic fibrosis, or highly penetrant disorders. Gene-mapping studies have identified three genes that, in certain mutant variants, are linked to a 100 percent chance of developing early-onset Alzheimer disease,[279] but attempts to identify less penetrant gene variants linked to psychiatric disorders have not been as successful. Although data continue to support a significant genetic susceptibility component to psychiatric disorders such as bipolar disorder and schizophrenia,[280] some early claims for familial genetic susceptibility markers for these disorders were retracted because they did not hold up with further study.[281]

Media attention to these earlier unsubstantiated reports, along with the potential for stigmatization based on research claims, prompted some commentators to propose slowing the pace of research and developing more stringent criteria for conducting behavioral genetics research and releasing research results to the press.[282] The American

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studies and some of the controversies linked to them, see also L. Wright, *Twins and What They Tell Us about Who We Are* (New York: John Wiley & Sons, 1997).

[276] Sherman et al., "Recent Developments in Human Behavioral Genetics," 1265.

[277] See Beckwith and Alper, "Human Behavioral Genetics," 5.

[278] For discussion of gene-mapping, see Chapter 1, page 23.

[279] Owen and Cardno, "Psychiatric Genetics," 11. The three genes linked to early-onset Alzheimer disease are called APP (beta amyloid precursor protein), PS-1 (presenilin-1), and PS-2 (presenilin-2). Early-onset Alzheimer disease is rare and distinct from the more common late-onset form of Alzheimer disease, which is not a single-gene disease. See Chapter 3, page 67.

[280] Berrettini, "Genetics of Psychiatric Disease," 465. Berrettini claims that the genetic component for disorders such as bipolar disorder is substantial, that susceptible individuals likely inherit several disease-predisposing gene variants, each incrementally increasing risk for a disorder, and that the role of environmental factors is always substantial.

[281] S. O. Moldin, "The Maddening Hunt for Madness Genes," *Nature Genetics* 17 (1997): 127; for a discussion of the problems for gene-mapping for disorders that have only moderate or low penetrance, see Owen and Cardro, "Psychiatric Genetics," 11–13.

[282] Moldin, "The Maddening Hunt for Madness Genes," 128; Beckwith and Alper, "Human Behavioral Genetics," 8; D. Wertz and R. Gregg, "Optimizing Genetics Services on a Social, Ethical, and Policy

Society of Human Genetics and others acknowledge these concerns but also emphasize the immense potential of behavioral genetics to identify both genetic and environmental influences on behavior and mental health.[283]

*Animal Model Studies*

Once human gene-mapping studies provide evidence that a particular gene may influence a behavioral trait, researchers can create new strains of genetically modified "transgenic" animals in attempts to study the role of specific genetic variations for particular behaviors.[284] Scientists have created strains of transgenic mice in which a specifically targeted gene, the mouse homologue of its human counterpart, is modified, added, or deleted. Transgenic mouse models have shown that modification or deletion ("knockout") of a particular gene may affect behaviors such as aggressiveness, exploratory activity, and anxiety-related behavior.[285] Some researchers have discovered, however, that mouse behavioral studies (for example, measuring exploratory activity in a mazelike structure) using the same transgenic mouse strains in different laboratories, under seemingly identical conditions, may yield different results.[286] These findings emphasize the potential importance of even relatively minor environmental factors on behaviors, the importance of standardizing laboratory studies, and the need for cautious interpretation of studies.[287] Other commentators point to the difficulty of measuring higher cognitive traits in animal models.[288]

***Outlook for Behavioral Genetics***

By highlighting the complex influence of genetic and environmental factors on behaviors, molecular genetics research has recast the nature-nurture debate from a competitive to an interactive model. While genetics research may provide important information about genetic contributions to behavior, it also points to the multiplicity of genes and environmental factors that contribute to complex traits.[289] One commentator states that

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Context: Suggestions from Consumers and Providers in the New England Regional Genetics Group," *The Genetic Resource* 10, no. 2 (1996): 59.

[283] Sherman et al., "Recent Developments in Human Behavioral Genetics," 1273–1274; Owen and Cardro, "Psychiatric Genetics," 14.

[284] O. Smithies, "Animal Models of Human Genetic Diseases," *Trends in Genetics* 9 (1993): 112. For a discussion of transgenic mice, see Chapter 1, page 22.

[285] J. C. Shih, K. Chen, and M. J. Ridd, "Monoamine Oxidase: From Genes to Behavior," *Annual Review of Neuroscience* 22 (1999): 197; D. Wahlsten, "Single-Gene Influences on Brain and Behavior," *Annual Review of Psychology* 50 (1999): 599; P. Timpl et al., "Impaired Stress Response and Reduced Anxiety in Mice Lacking a Functional Corticotropin-Releasing Hormone Receptor 1," *Nature Genetics* 19 (1998): 162.

[286] M. Enserink, "Fickle Mice Highlight Test Problems," *Science* 284 (1999): 1599.

[287] Ibid.

[288] Owen and Cardro, "Psychiatric Genetics," 13.

[289] Plomin, "Genetics and General Cognitive Ability," C28; see also J. D. McInerney, "Genes and Behavior: A Complex Relationship," *Judicature* 83 (1999), U.S. Department of Energy Human Genome Project Information website: *http://www.ornl.gov/hgmis/publicat/judicature/article4.html*, visited March 9, 2000.

to ask whether nature or nurture is more important is "fallacious and misleading";[290] another refers to the debate as an "exploded myth."[291]

Still, many predict that genetic components of human behavior and cognition will be defined and may become subject to genetic testing, with attendant social and ethical implications of such testing. One commentator, discussing general cognitive ability, states that the many genes (and their variants) that contribute to particular cognitive traits such as memory and reading ability will be identified and that this may lead to development of a "DNA chip" for use "in education to consider how far children are fulfilling their genetic potential or to prescribe different training programmes."[292]

### *Genetic Essentialism: The Gene as Cultural Icon*

Complexity is not easily embraced by popular culture. Simplistic and misleading references to genes and to DNA abound, as reflected in entertainment, advertising, social discourse, and news stories. In their 1995 book entitled *The DNA Mystique: The Gene as Cultural Icon*, authors Dorothy Nelkin and M. Susan Lindee cite a long list of examples.[293] In the popular press and on television, individual personalities, behaviors, and criminal tendencies are discussed in terms of "empathy genes," "selfish genes," "frugality genes," "gay genes," and "violence genes."[294] Product advertisements tout the superior "DNA" of inanimate commodities such as magazines and cars.[295] The authors opine that the biological gene has taken on a cultural meaning as a powerful social symbol, a "secular equivalent of the human soul."[296] Another commentator states that genes have become the "metaphorical locus of our fate"[297] and notes that the Human Genome Project may be perceived as the new "key" to decoding the "hidden truths of existence," an idea with which Western culture has shown a "long flirtation."[298]

Scientists themselves, inadvertently or otherwise, also may promote overly deterministic perceptions, referring to the human genome as a "Delphic oracle," "medical crystal ball," or "Book of Man."[299] This blending of scientific and social discourse, as occurred earlier in the century, led in the 1990s to what Nelkin and Lindee coined "genetic

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[290] Reilly, "A Look Back at Eugenics" (quoting Columbia University scientist Theodosius Dobshansky).
[291] G. S. Omenn, "Comment: Genetics and Public Health," *American Journal of Public Health* 86 (1996): 1701.
[292] Plomin, "Genetics and General Cognitive Ability," C29.
[293] Ibid.; see also D. Nelkin, "Behavioral Genetics and Dismantling the Welfare State," in *Behavioral Genetics — The Clash of Culture and Biology*, 156.
[294] Nelkin and Lindee, *The DNA Mystique*, 2, 99.
[295] Ibid., 97.
[296] Ibid., 2.
[297] Wolpe, "If I Am Only My Genes, What Am I?" 217.
[298] Ibid., 219.
[299] Ibid., 216–217; Nelkin and Lindee, *The DNA Mystique*, 7–8.

essentialism," the equating of individuals with their genes.[300] Others have used the terms "genomania"[301] and "geneticization"[302] in reference to the current trend of popular thought concerning genetic determinism. One commentator suggests that today's greater "scientific certainty" and the highly technical terminology of molecular genetics stir considerable fear among the general public, possibly of a greater magnitude than previously.[303] This fear of DNA and genes rests on the notion that geneticists have discovered the "ultimate building blocks that make us what we are."[304]

In the United States, some express concern that the legal and judicial systems also are embedded in an overly determinist view of humanity. One commentator expresses concern that while the Supreme Court has generally declared as legally suspect laws that discriminate on the basis of "immutable" characteristics, such as race or sex,[305] it has been less concerned with environmental circumstances over which an individual may have little or no control, "such as a history of abuse, poor education, or economic impoverishment."[306] Another commentator points to manifestation of this determinist view in child custody cases, where courts may generally privilege biological over nonbiological parenting relationships, even at the expense of the "best interests of the child."[307]

## *Public Perceptions and Misperceptions about Medical Genetic Testing*

Genetic essentialism, coupled with a generally poor public grasp of genetics, probability, and risk analysis,[308] can lead to misperceptions about the value of genetic testing and the meaning of medical genetic test results. Some health care professionals express concern that the rapid spread of information about genetic testing without adequate education may be inappropriately raising patients' expectations.[309] One area in which marketing and media stories may have led some individuals to misperceive their

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[300] Nelkin and Lindee, *The DNA Mystique*, 41.
[301] Hubbard and Wald, *Exploding the Gene Myth*, 164.
[302] A. Lippman, "Prenatal Genetic Testing and Screening: Constructing Needs and Reinforcing Equities," *American Journal of Law and Medicine* 17 (1991): 15.
[303] Wertz, "What Are We Afraid Of?" 300–301, 307.
[304] Ibid., 307.
[305] See, e.g., *Frontiero vs. Richardson*, 411 U.S. 677, 93 Ct. 1764 (1973).
[306] D. L. Burk, "Genetic Testing's Political Implications Must Be Addressed," *The Scientist*, July 21, 1997, 8.
[307] Wertz, "Society and the Not-So-New Genetics," 308; New York State Task Force on Life and the Law, *Assisted Reproductive Technologies: Analysis and Recommendations for Public Policy* (New York: New York State Task Force on Life and the Law, 1998), 342–345.
[308] S. T. Bogardus, E. Holmboe, and J. J. Jekel, "Perils, Pitfalls, and Possibilities in Talking about Medical Risk," *Journal of the American Medical Association* 281 (1999): 1037; N. D. Weinstein, "What Does It Mean to Underestimate a Risk? Evaluating Risk Comprehension," *Journal of the National Cancer Institute* (Monograph No. 25), 1999, 15; B. A. Bernhardt et al., "Educating Patients about Cystic Fibrosis Carrier Screening in a Primary Care Setting," *Archives of Family Medicine* 5 (1996): 336.
[309] "Genetic Medicine — Jumping to Conclusions," quoting Dr. Sharon Plon, cancer genetics researcher at Baylor College of Medicine, Howard Hughes Medical Institute website: *http://hhmi.org/genmed/jumping.htm*, visited July 15, 1998.

genetic risk is that of genetic susceptibility to breast cancer and BRCA gene testing.[310] For example, one study showed that among a group of 200 women with breast/and or ovarian cancer, 60 percent overestimated their chance of having a BRCA gene mutation.[311] In other studies, many women who had relatives affected by breast cancer overestimated their personal risk for developing breast cancer or having a BRCA gene mutation.[312] Others have expressed concerns that patients sometimes respond inappropriately to news stories by seeking radical treatments such as prophylactic mastectomy.[313]

Some concerns are rooted in the public's weak grasp of scientific concepts generally.[314] Several studies point to a weakness in understanding risk and probability, which is critical for understanding the role of susceptibility gene variants for late-onset disorders and for some types of prenatal and carrier testing. In one study, researchers presented women with a clinical scenario and asked them to choose which of a pair of probability estimates represented a higher risk.[315] The probabilities were presented either as a pair of rates per 1,000 (2.6/1,000 versus 8.9/1,000) or as a proportional ratio in which the numerator was one and the denominator was varied (1/112 versus 1/384). Over one-quarter of women surveyed incorrectly judged which of the numbers in either pair posed a higher risk.[316]

For many persons, it is a challenge to reconcile an average derived from populations and its meaning for them individually.[317] Some have a binary, simplistic view of risk.[318] This overly simplistic understanding may give rise to a false sense that genetic test results always provide absolute predictability. Even physicians may experience difficulty in correctly interpreting predictive genetic test results. For example, in one study a researcher asked a group of medical students, interns, and practicing

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[310] S. Lehrman, "Should You Get the Breast Cancer Gene Test?" *Health* (November/December 1998): 129, 130.

[311] L. G. Bluman et al., "Attitudes, Knowledge, and Risk Perceptions for Women with Breast and/or Ovarian Cancer Considering Testing for BRCA1 and BRCA2," *Journal of Clinical Oncology* 17 (1999): 1040.

[312] See R. T. Croyle and C. Lerman, "Risk Communication in Genetic Testing for Cancer Susceptibility," *Journal of the National Cancer Institute* (Monograph No. 25), 1999, 59–60; see also J. M. Elwood, "Public Health Aspects of Breast Cancer Gene Testing in Canada. Part 2: Selection for and Effects of Testing," *Chronic Diseases in Canada* 20 (1999): 14.

[313] "Genetic Medicine — Jumping to Conclusions."

[314] "Editorial: Connect," *Nature Genetics* 19 (1998): 305 (discussing results of a 1998 National Science Foundation survey).

[315] D. A. Grimes and G. R. Snively, "Patient's Understanding of Medical Risks: Implications for Genetic Counseling," *Obstetrics and Gynecology* 93 (1999): 910.

[316] Ibid. When the pair of probabilities was presented as proportions, 56 percent guessed correctly; when presented as rates, 73 percent answered correctly.

[317] Bogardus, Holmboe, and Jekel, "Perils, Pitfalls, and Possibilities," 1040.

[318] Grimes and Snively, "Patient's Understanding of Medical Risks," 910.

physicians to calculate the positive predictive value of a hypothetical genetic test.[319] While 86 percent of medical students could correctly identify, from a set of multiple choice answers, the chance that an individual who tested positive actually would get a given disease, only 48 percent of practicing physicians answered correctly.[320]

Other factors also influence how individuals perceive risk estimations. Perceptions about health risks are multidimensional, encompassing not only the probability but also the seriousness of the harm, the availability of preventive measures, and the ease or difficulty of employing such measures.[321] While misperception of risk is relevant for all medical risk assessment, one commentator opines that genetic essentialism may compound this problem for genetic testing.[322]

Another important factor is a person's tolerance, or intolerance, for uncertainty. In a survey of women undergoing prenatal genetic testing, the willingness of women to abort an affected fetus increased dramatically as the certainty of the diagnosis reached 100 percent, even when the prognosis was highly variable.[323] Another study showed that decisions to undergo prenatal carrier testing for cystic fibrosis were strongly influenced by the patient's tolerance for uncertainty and that this level of tolerance was unrelated to either educational background or attitudes about prenatal testing and abortion.[324] For adult-onset genetic cancer susceptibility testing, one study showed that women with low tolerance for uncertainty who were considering testing for a susceptibility mutation made different testing decisions depending on whether the informed consent document stated that some cancer risk remained for those testing negative.[325]

## Eugenic Concerns

### *Coercive Policies and Laws*

There is little evidence of systematic, coercive eugenic practice in the world today. Eugenic laws exist in three countries — Singapore, Taiwan, and China — but they lack penalties and there is no evidence of their enforcement.[326] China's 1994 law, however, has

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[319] For a discussion of positive predictive value, see Chapter 2, page 41.

[320] N. A. Holtzman, "Bringing Genetic Tests into the Clinic," *Hospital Practice*, January 19, 1999, 107, 125. Most physicians who answered incorrectly selected a predictive value of 95 percent, versus the correct answer of 2 percent.

[321] Weinstein, "What Does It Mean to Understand a Risk?" 15, 16.

[322] M. Lappe, "The Limits of Genetic Inquiry," *Hastings Center Report* 17, no. 4 (1987): 5, 8. The author did not use the term genetic essentialism, which had not yet been introduced.

[323] Ibid., 8. The author cites a 1987 study that enrolled 193 married women. When prenatal diagnosis was presented as 100 percent certain but the severity of the prognosis variable, 24 percent more women would elect abortion than when the diagnosis had a 95 percent probability.

[324] N. A. Holtzman and L. B. Andrews, "Ethical and Legal Issues in Genetic Epidemiology," *Epidemiological Reviews* 19 (1997): 163, 169.

[325] R. T. Croyle et al., "Need for Certainty and Interest in Genetic Testing," *Women's Health* 1 (1995): 329.

[326] Wertz, "State-Controlled Eugenics in the Postmodern World"; American Society of Human Genetics, "Eugenics and the Misuse of Genetic Information."

received international attention.[327] Some interpret as coercive a provision of the law to require sterilization or long-term contraception and/or prenatal diagnoses for couples determined to be at hereditary risk for bearing an affected child. Chinese officials argue that this interpretation is due to flawed translation.[328] Concerns about the law, however, prompted participants at the 1998 International Congress of Genetics, convened in Beijing, China, to issue a statement that affirms the centrality of informed individual choice and genetic counseling in prenatal genetic testing decisions.[329]

In the United States, even though the Supreme Court declared antimiscegenation laws unconstitutional in 1967,[330] two states retained laws forbidding interracial marriages in their constitutions until 1998.[331] Some states also retain compulsory sterilization laws,[332] although these laws are subject to constitutional constraints.[333] In the 1960s and 1970s, however, many states, in part attempting to redress past eugenic policies, repealed eugenic sterilization laws and, in some cases, enacted legislative barriers to sterilization of mentally impaired[334] persons.[335] Some states banned all sterilization of incompetent persons,[336] and in several other states, courts effectively banned sterilization by refusing to allow such

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[327] See, e.g., American Society of Human Genetics, "Eugenics and the Misuse of Genetic Information."

[328] B. M. Knoppers, "Well-Bear and Well-Rear in China?" *American Journal of Human Genetics* 63 (1998): 686.

[329] Normile, "Geneticists Debate Eugenics," 1118; "GeneLetter — 18th International Congress of Genetics Statement on Eugenics," *The Gene Letter* (February 1999), website: *http://www.geneletter.org*, visited June 7, 1999; D. Dickson, "Congress Grabs Eugenics Common Ground," *Nature* 394 (1998): 711.

[330] *Loving v. Virginia,* 388 U.S. 1, 2, 87 S. Ct. 1817, 1818 (1967). In this case, the Supreme Court reversed a Virginia conviction of a one-year jail sentence for a married couple charged with violating Virginia's ban on interracial marriages.

[331] B. Staples, "Editorial Observer: The Final Showdown on Interracial Marriage," *New York Times*, July 6, 1999, New York Times website: *http://graphics.nytimes.com/images*, visited July 13, 1999. Voters removed South Carolina's law in 1998, and a similar referendum to remove Alabama's law was initiated in 1999. Enforcement of antimiscegenation laws would clearly be unconstitutional.

[332] Kevles, *In the Name of Eugenics*, 111. For example, a North Carolina law authorizes petitions for sterilization of any "mentally ill or retarded person" and for "persons likely to procreate a child or children who probably would have serious physical, mental or nervous diseases or deficiencies." Also, the law rests on the "public good" rather than on the best interests of the individual for whom sterilization is considered. N. C. Gen. Stat. §§ 35–36 (1999). See also J. Zumpano-Canto, "Nonconsensual Sterilization of the Mentally Disabled in North Carolina: An Ethics Critique of the Statutory Standard and Its Judicial Interpretation," *Journal of Contemporary Health Law and Policy* 13 (1996): 79.

[333] Enforcement of compulsory sterilization laws might raise constitutional concerns in light of the Supreme Court's 1942 decision in *Skinner v. Oklahoma*, which recognized reproduction as "one of the basic civil rights of man." 316 U.S. 535, 541, 62 S. Ct. 110, 113 (1942).

[334] Different sources use as interchangeable the terms "mentally impaired," "mentally disabled," "mentally retarded," and "mentally handicapped."

[335] See E. S. Scott, "Sterilization of Mentally Retarded Persons: Reproductive Rights and Family Privacy," *Duke Law Journal* (1986): 806, 809. In 1979, federal regulations denied the use of federal funds for the sterilization of any incompetent person. 42 C.F.R. § 50.201 (1999).

[336] For example, in 1981, California, the state with the largest number of involuntary sterilizations up to 1963, enacted a law barring the sterilization of minor incompetents. Cal. Prob. Code § 2356(d) (Deering 1981). See Scott, "Sterilization of Mentally Retarded Persons," 817.

procedures in the absence of statutory authority.[337] In some cases, laws forbidding sterilization have precluded sterilization even when it is arguably in the best interests of a severely mentally impaired girl or woman.[338]

Other states, by statute or judicial decisions, sanction the state's *parens patriae* power to authorize sterilization of a mentally impaired person, generally under strict requirements that create a strong presumption against sterilization and seek to assure the best interests of the impaired person.[339] For example, in 1981, the New Jersey Supreme Court established conditions under which a court may authorize the sterilization of a severely mentally impaired woman.[340] A 1988 committee opinion issued by the American College of Obstetricians and Gynecologists also allows for sterilization of mentally impaired women under some circumstances.[341] The statement declares that nonvoluntary sterilization is generally not ethically acceptable but that in unusual situations, "sterilization may be considered a reasonable part of the overall health care of a person who is mentally incapacitated or incompetent." Key factors are: (1) protecting the best interests of the woman, (2) identification of appropriate decision-makers, (3) consideration of alternatives to sterilization,[342] and (4) understanding of applicable laws.[343]

### *Noncoercive Policies*

Even in the absence of coercive laws, voluntary governmental programs and policies may promote or discourage certain types of births.[344] In such cases, the rationales used are the same as those for more overt eugenic policies: improved public health and "fairer" distribution of limited public resources. One example is a 1972–1983 government-sponsored carrier screening program for beta-thalassemia in Cyprus. In this program, educators counseled prospective parents to follow a prenatal diagnosis by

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[337] Scott, "Sterilization of Mentally Retarded Persons," 817. See, e.g., *Wade v. Bethesda Hosp.,* 337 F. Supp. 671, 673–674 (S.D. Ohio 1971); *Hudson v. Hudson*, 373 So. 2d 310, 312 (Ala. 1979).

[338] Scott, "Sterilization of Mentally Retarded Persons," 817. In some cases, these laws were later struck down. For example, California's law was struck down in 1985. *Conservatorship of Valerie N.*, 40 Cal. 3d 143, 160–161, 707 P.2d 760, 771–772, 219 Cal. Rptr. 387, 398–399 (1985).

[339] Scott, "Sterilization of Mentally Retarded Persons," 817–819. *Parens patriae* authority permits the state to intervene to protect children from substantial and imminent harm. One example, Maine's law, requires "clear and convincing evidence that sterilization is in the best interest of the person being considered for sterilization." Me. Rev. Stat. Ann. Tit. 34-B § 7013(4) (West 1998). Earlier state laws allowing sterilization were grounded not in the state's *parens patriae* but in its police power. See Scott, "Sterilization of Mentally Retarded Persons," 819–820.

[340] *Grady v. Supreme Court of New Jersey*, 85 N. J. 235, 263–267, 426 A.2d 467, 482–483 (1981).

[341] American College of Obstetricians and Gynecologists, "ACOG Committee Opinion: Sterilization of Women Who Are Mentally Handicapped," ACOG Committee Opinion No. 63 (Washington, D.C., 1988). The statement was endorsed by the American Academy of Pediatrics. American Academy of Pediatrics Committee on Bioethics, "Sterilization of Women Who Are Mentally Handicapped (RE9180)," *Pediatrics* 85 (1990): 868. The professional statements address sterilization of females only.

[342] The ACOG Committee Opinion notes that while noninvasive modalities should be considered, "the risks associated with long-term medical contraception or hormonal treatment may be as great or greater than those of a single definitive surgical treatment." American College of Obstetricians and Gynecologists, "ACOG Committee Opinion: Sterilization of Women Who Are Mentally Handicapped."

[343] Ibid.

[344] A. Nordgren, "Reprogenetics Policy: Three Kinds of Models," *Community Genetics* 1 (1998): 61, 63.

selective abortion.[345] Cost-effectiveness studies that justify a reduction in the births of infants affected by particular disorders, especially when embraced by government, also may exert eugenic pressures.[346] For example, in the early 1990s, supporters of a Colorado school-sponsored genetic screening program to detect children with the genetic disorder Fragile X, which may be associated with mental retardation, suggested that the screen, coupled with reproductive counseling, could reduce the state's disease-associated "economic burden."[347]

Even in the absence of a direct state role, some claim that more subtle cultural, social, legal, and economic pressures may promote a passive or indirect form of eugenics. For example, some courts have suggested that legal recognition of wrongful birth or wrongful life lawsuits, in which parents claim they would not have initiated or continued a pregnancy if their physician had offered, performed, and correctly interpreted a reproductive test to detect a congenital disorder, may send a eugenic message.[348] One commentator argues that limited access to health care of some social and economic classes leads to a form of "passive eugenics" within the United States.[349] Another uses the term "backdoor eugenics" to describe potential harms posed to individuals or groups by the cumulative effects of private decisions of many societal sectors, including insurers and employers.[350]

Another source of concern is the expanding range of reproductive tests and procedures that, unlike the original model for reproductive testing, allows testing for less serious disorders. The new tests and procedures, including pre-implantation genetic diagnosis of embryos[351] and "sorting" of sperm for sex selection,[352] allow prospective parents to test not only for single-gene disorders but also for health risk factors (susceptibility mutations)[353] and traits, including sex. Some commentators also point to a future genetic engineering-based form of positive eugenics, or genetic "enhancement" of embryos by insertion of genes to improve particular characteristics or disease resistance into the embryo's genome.[354]

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[345] Ibid., 65.
[346] K. L. Garver and B. Garver, "The Human Genome Project and Eugenic Concerns," *American Journal of Human Genetics* 54 (1994): 148, 153.
[347] See P. Billings and R. Hubbard, "Fragile X Testing: Who Benefits?" *Gene Watch* 9 (1994): 1, 2.
[348] See, e.g., *Baylor v. Kurapati*, 236 Mich. App. 315, 349–355, 600 N.W. 2d 670, 688–691 (1999).
[349] J. E. Bowman, "The Road to Eugenics," *University of Chicago Law School Roundtable* 3 (1996): 491, 493.
[350] T. Duster, *Backdoor to Eugenics* (New York: Routledge, 1990).
[351] See Chapter 3, page 53.
[352] See Chapter 3, page 55.
[353] See Chapter 3, page 62.
[354] See, e.g., L. M. Silver, *Remaking Eden — Cloning and Beyond in a Brave New World* (New York: Avon Books, 1997), 237–239.

Other commentators express concerns about government proposals that seek to restrict reproduction generally for certain classes of people, for example, women receiving public assistance.[355] Several states have proposed and/or passed legislation that would provide financial rewards to women who accept surgical implantation of Norplant, a long-term contraceptive device.[356] While supporters of these programs do not argue, as earlier eugenic advocates did, that social status is genetically determined, commentators claim that the programs' aims are eugenic.[357] These commentators note that the Norplant bonus policy aims to deny procreative rights to a class of people whom the media and others falsely portray as responsible for social ills based on stereotypes grounded in racism, classism, and sexism. Others have expressed concerns about overly directive offering of prenatal screening tests,[358] the influence of cultural agendas and notions of normality and disability on testing decisions,[359] and the inappropriateness of offering prenatal testing to women who lack the full range of information and options for acting on test results.[360]

### *Misuse of Genetic Information to Target Races and Social Classes*

Another concern is that genetic information will be misused outside of direct reproductive decisions, intentionally or unintentionally, to discriminate against racial, ethnic, and social classes. A major concern is that genetic information that may be reliable on an individual basis may be inappropriately extended to describe groups.[361] This concern is stirred by the potential for misuse of expanding genetics research in behavior and cognition.[362] One commentator referred to modern behavioral genetics as

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[355] See M. G. Broomfield, "Controlling the Reproductive Rights of Impoverished Women: Is This the Way to 'Reform' Welfare?" *Boston College Third World Law Journal* 16 (1996): 217, 232–233; L. C. Nolan, "The Unconstitutional Conditions Doctrine and Mandating Norplant for Women on Welfare Discourse," *American University Journal of Gender and Law* 3 (1994): 15, 21–22; D. Roberts, *Killing the Black Body — Race, Reproduction, and the Meaning of Life* (New York: Pantheon Books, 1997).

[356] Norplant is a method of birth control consisting of six matchstick size capsules that are surgically implanted in a woman's arm, providing time release of a synthetic hormone. It is effective for prevention of pregnancy over a five-year period and requires surgical removal. See P. D. Darney, "Hormonal Implants: Contraception for a New Century," *American Journal of Obstetrics and Gynecology* 170 (1994): 1536; see also Nelkin and Lindee, *The DNA Mystique*, 186–187. For a discussion of Norplant and issues surrounding state policies to promote its use, see Roberts, *Killing the Black Body*, 104–149.

[357] Broomfield, "Controlling the Reproductive Rights of Impoverished Women," 220; Nolan, "The Unconstitutional Conditions Doctrine and Mandating Norplant," 32.

[358] For a discussion of directive versus nondirective offering of and counseling for prenatal genetic tests, see Chapter 12, page 349.

[359] See E. Parens and A. Asch, "The Disability Rights Critique of Prenatal Genetic Testing," *Hastings Center Report* 29 suppl. (1999): S1; A. Asch, "Prenatal Diagnosis and Selective Abortion: a Challenge to Practice and Policy," *American Journal of Public Health* 89 (1999): 1649.

[360] Wertz, "Eugenics Is Alive and Well," 493; Wertz, "Eugenics: Definitions"; A. Lippman, "Choice in Prenatal Testing," *Gene Watch* 12 (June, 1999): 1.

[361] E. Parens, "Taking Behavioral Genetics Seriously," 16; R. Murray, "Genetics and Violence," in *Violence: from Biology to Society*, ed. J. S. Grisolia et al. (New York: Elsevier, 1997), 87, 93.

[362] Parens, "Taking Behavioral Genetics Seriously," 13.

"the same old stuff in new clothes. . . . It's another way for a violent, racist society to say people's problems are their own fault, because they carry 'bad' genes."[363]

For example, while evidence supports a complex hereditary influence on an individual's intelligence traits, critically tempered by social and other environmental factors, some may generalize and overextend genetic information to claim reduced heritable intelligence not only of individuals, but also of social classes and/or races. One commentator cites as an example the much-publicized 1994 book *The Bell Curve*.[364] The book's authors claim that intelligence levels, as measured by IQ testing, are highly heritable and linked to social class; they also warn of a potential drop in the national IQ if current class-based reproductive traits continue. While the book met considerable criticism, some also warn against overly "politically correct" views that fail to acknowledge that there are hereditary influences on intelligence and behavioral traits — as part of a complex and interactive process with cultural and other environmental factors.[365]

## Is Genetic Testing Different from Other Medical Testing?

Within the medical and policy communities, there is a debate about whether genetic testing and information are sufficiently different from other types of health-related testing and information to warrant special considerations or protections. One participant in this debate, the 1993 National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Information and Insurance, referred to the claim that medical genetics is sufficiently different to warrant special protections as "genetic exceptionalism."[366]

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[363] Ibid. (quoting Peter Briggin, Director, Center for the Study of Psychiatry, Bethesda, MD).

[364] D. C. Wertz, "Eugenics, Class, and IQ: The Bell Curve," in *The Gene Letter* (February 1999), website: *http://www.geneletter.org*, visited May 4, 1999 (reviewing R. Herrnstein's and Charles Murray's 1994 book *The Bell Curve: Intelligence and Class Structure in American Life*). See also Rothstein, "Behavioral Genetics Determinism," 94–95. For a discussion of the decades-long controversy about IQ testing as a measure of intelligence, see Kevles, *In the Name of Eugenics*, 77–80, 134–147.

[365] Parens, "Taking Behavioral Genetics Seriously," 16–17; Sherman et al., "Recent Developments in Human Behavioral Genetics," 1273–1274.

[366] National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Information and Insurance, *Genetic Information and Health Insurance* (Washington, D.C.: National Institutes of Health, 1993), National Human Genome Research Institute website: *http:// www.nhgri.gov/About_NHGRI/Der/Elsi/itf.html*, visited July 18, 2000.

### Definitions of Genetic Testing and Information

To address the claim of genetic exceptionalism, it is necessary first to establish definitions of genetic testing and information. Here, too, there is disagreement.[367] For example, a statement by joint organizations of pathologists uses a broad, clinically based definition of genetic testing as tests that "provide information used for diagnosing an inherited disorder."[368] Another group restricts the definition of genetic testing to tests performed on DNA.[369]

A broader, and yet more precise, scientifically based definition would define genetic testing as testing of an individual's inherited genes, gene products, or chromosomes to distinguish among heritable and specific variants of a designated gene or chromosome.[370] For example, a DNA-based test for sickle cell disease can distinguish precisely between two variants of the beta globin gene: the normal population variant and the disease-associated variant that differs by a single DNA base.[371] A test of an individual's beta globin protein (a "gene product") also distinguishes between the defined gene variants and therefore would also be considered a genetic test. However, whereas a DNA-based test to distinguish a particular gene variant associated with inherited familial hypercholesteremia would be considered a genetic test, under this definition, a simple serum cholesterol test would not be. A person's serum cholesterol measure changes over time and is affected by complex and interactive genetic and environmental factors, including diet and weight. It provides no definitive information about a particular inherited gene variant.

Genetic information can be defined as specific information about a person's inherited genetic variations. Genetic information generally is learned by genetic testing, although it might be learned by other means. For example, parents of a child with cystic fibrosis know they carry a mutation in the gene associated with the disease.

### How Are Genetic Testing and Information Different?

Genetic testing and information differ from other health-related testing and information, in kind or in degree, by a number of different, sometimes overlapping qualities, outlined below. Some qualities apply only to DNA-based testing, which is the most frequently used testing technology.[372]

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[367] See, for example, K. H. Rothenberg, "Genetic Information and Health Insurance: State Legislative Approaches," *Journal of Law, Medicine, and Ethics* 23 (1995): 312, 313.

[368] W. Grizzle et al., "Recommended Policies for Uses of Human Tissue in Research, Education, and Quality Control," *Archives of Pathology and Laboratory Medicine* 123 (1999): 296, 297.

[369] G. J. Annas, L. H. Glantz, and P. A. Roche, "Drafting the Genetic Privacy Act: Science, Policy, and Practical Considerations," *Journal of Law, Medicine and Ethics* 23 (1995): 360.

[370] See Chapter 2, page 29. This includes testing to determine differences in type (e.g., different variants [alleles] of the same gene, or an XX versus XY chromosome genotype) or number (e.g., a missing or extra copy of a particular gene or chromosome).

[371] See Chapter 2, page 35. DNA-based testing also can detect other variants of the same gene.

[372] See Chapter 2, page 31.

### *Predictive Power of Genetic Information*

Many medical tests, including serum cholesterol and blood pressure measures, can predict future health risks. However, genetic testing has more far-reaching predictive powers. It can indicate an individual's risk probabilities for late-onset disorders many decades before the presence of clinical signs or symptoms; reproductive genetic testing can predict the same risks for an embryo, a fetus, or an individual's future offspring. A recent task force decided that testing healthy people to predict future illness is "the most unique and troublesome aspect of genetic testing."[373]

### *Stability of DNA*

The stability of DNA is a fundamental difference between DNA-based genetic testing and other medical testing. Information determined by genetic testing of inherited gene variants of a newborn infant will not change over that infant's lifetime, while medical signs and symptoms detected by other medical tests may. Samples may be stored indefinitely, enabling testing of long-deceased individuals.

### *Limited Sample Requirement*

Another unique aspect of DNA-based genetic testing is that it can be performed with tiny samples, as little as a single cell. This allows predictive testing of pre-implantation embryos and forensic testing with microscopic tissue samples.[374] For example, following the terrorist bombing of the World Trade Center in New York City, the Federal Bureau of Investigation was able to identify a suspect by testing DNA from the back of a stamp (from cells shed into saliva) on a letter that claimed credit for the bombing.[375]

### *Precision of Genetic Information*

Genetic testing, by detection of specific gene variants, has a very high capacity for precision. In some cases, for example DNA-based cystic fibrosis testing, detection of particular gene mutations may enable prediction not only of the disorder, but also of the

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[373] National Institutes of Health-U.S. Department of Energy Joint Working Group on the Ethical, Legal, and Social Implications of the Human Genome Project Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing,* ed. N. A. Holtzman and M. S. Watson (Bethesda: National Institutes of Health, 1997); see also N. A. Holtzman, "Panel Comment: The Attempt to Pass the Genetic Privacy Act in Maryland," *Journal of Law, Medicine, and Ethics* 23 (1995): 367, 369.

[374] For discussion of genetic testing of pre-implantation embryos, see Chapter 3, page 53. For discussion of forensic DNA-based testing, see Chapter 2, page 31.

[375] T. H. Murray, "Genetic Exceptionalism and Future Diaries: Is Genetic Information Different from Other Medical Information?" in *Genetic Secrets: Protecting Privacy and Confidentiality in a Genetic Era*, ed. M. A. Rothstein (New Haven, CT: Yale University Press, 1997), 60.

type and severity of the disorder.[376] For more complex disorders, testing for inherited susceptibility variants can provide precise information about innate risk, although it cannot predict that a person will develop a disorder. The level of precision of genetic tests is greater than that of most other medical tests.

### *Personal Nature of Genetic Information*

Genetic testing of health-related or other DNA "markers" that vary among the population can theoretically produce a "unique identifier" profile for any person.[377] This is the basis for DNA-based forensic testing, which can identify a single individual from millions of others.[378] Some view this difference of genetic information as qualitatively different from other health data.[379] One commentator, however, claims that some nongenetic data in a medical record, such as gross obesity and loss of limbs, also may serve to identify an individual.[380] He also suggests that the "considerable work and expense" needed to compile an identifying genetic profile would act as a deterrent to the use of genetic information in this manner,[381] but evolving technologies may eventually render this claim obsolete.[382]

### *Familial Nature of Genetic Information*

Genetic information, while personal, also is inherently familial. Identical twins share 100 percent of their genes, other siblings (and a parent and a child) share 50 percent, and more distant relatives share a lower but calculable percentage of genes. Genetic testing, including blood group antigen testing and tissue typing to match donors and recipients for tissue transplantation, also may reveal nongenetic relationships within families, such as nonpaternity.

While other medical information also may help identify shared family risks, for example, information about infectious disease, the level of precision of genetic testing places genetic information at a significantly different level. One example of the power of genetic testing to disclose family relationships: Genetic testing of living descendants of Thomas Jefferson and descendents of one of his slaves, Sally Hemings, established Jefferson, or one of his nephews, as the father of at least one of Hemings' sons 200 years earlier.[383]

## ***History of Misuse and Misunderstanding of Genetics***

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[376] T. Brown and E. Langfelder Schwind, "Update and Review: Cystic Fibrosis," *Journal of Genetic Counseling* 8 (1999): 137; see also Chapter 5, page 119.
[377] L. O. Gostin, "Genetic Privacy," *Journal of Law, Medicine, and Ethics* 23 (1995): 320, 322.
[378] See Chapter 2, page 31.
[379] Gostin, "Genetic Privacy," 322.
[380] Murray, "Genetic Exceptionalism," 64.
[381] Ibid.
[382] See, e.g., Chapter 2, page 45.
[383] E. S. Lander and J. J. Ellis, "Founding Father," *Nature* 396 (1998): 13.

Some think that past misuse of genetic information to stigmatize and victimize people is another factor that sets genetic information apart from other medical information.[384] One commentator states that claims for genetic exceptionalism are partly due to a cultural overemphasis on the power of genetic information.[385] Another group counters that public misperceptions about the power of genes may be a reason to treat genetic information differently from other medical information.[386]

### *Inadequate Provider Education*

Many commentators claim that the new era of genomic medicine poses a unique challenge to the practice of medicine because of the insufficient genetics education of most primary care providers.[387] For example, Dr. Francis Collins, Director of the National Institute of Human Genome Research, predicts that genetic medicine will need to be practiced in part by primary care providers, even though numerous surveys show that most of them "have not had a single hour of instruction in genetics as part of their formal training."[388]

## Policy Implications

Commentators disagree on whether public policy should treat genetic tests as fundamentally different from other types of medical tests. The Task Force on Genetic Information and Insurance, for example, concluded that, because it is impossible to categorize all diseases and risk factors as either "genetic" or "nongenetic," a policy of genetic exceptionalism would be unworkable in practice.[389] Others maintain that the risks associated with genetic testing are in a "qualitatively different realm" than associated with other tests[390] or argue that, even if genetics is not unique, it may be distinctly different from other areas of

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[384] A. R. Jonsen et al., "The Advent of the 'Unpatients,'" *Nature Medicine* 2 (1996): 622; R. M. Green and A. M. Thomas, "DNA: Five Distinguishing Features for Policy Analysis," *Harvard Journal of Law and Technology* 11 (1998): 571, 584; G. J. Annas, "Privacy Rules for DNA Databanks: Protecting Coded 'Future Diaries,'" *Journal of the American Medical Association* 270 (1993): 2346.

[385] Murray, "Genetic Exceptionalism," 70.

[386] G. Geller et al., "Consensus Statement — Genetic Testing for Susceptibility to Adult-Onset Cancer," *Journal of the American Medical Association* (1997): 1467.

[387] F. S. Collins, "Shattuck Lecture — Medical and Societal Consequences of the Human Genome Project," *New England Journal of Medicine* 341 (1999): 28, 35; Geller et al., "Genetic Testing for Susceptibility to Adult-Onset Cancer," 1468. See also Chapter 12, page 362.

[388] Collins, "Medical and Societal Consequences of the Human Genome Project," 35.

[389] Murray, "Genetic Exceptionalism," 67.

[390] Green and Thomas, "DNA: Five Distinguishing Features," 576.

> medicine.[391] For example, The Cancer Genetics Studies Consortium (CGSC) Task Force on Informed Consent found that genetic information about susceptibility to adult-onset cancer is more complex than other types of medical information because it simultaneously affects an entire family, is laden with symbolic meaning, and presents unique challenges to insufficiently educated medical personnel.[392]

One possible approach to this problem is to consider whether genetic testing is different from other medical testing on an issue-by-issue basis, rather than debating whether genetics is inherently unique. For example, the CGSC Task Force on Informed Consent decided that for informed consent for predictive cancer susceptibility gene testing, genetic information differs sufficiently from other medical information in several key qualities and, based on those differences, requires special considerations.[393] Others have considered, and disagreed about, whether genetic information warrants special confidentiality concerns.[394] Additional policy and practice areas for which this question may be addressed include insurance coverage, employment issues, predictive genetic testing of children, and genetic research use of tissue samples.[395]

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[391] Ibid., 576; Annas, Glantz, and Roche, "Drafting the Genetic Privacy Act," 365; Geller et al., "Genetic Testing for Susceptibility to Adult-Onset Cancer," 1468; Jonsen et al., "The Advent of the 'Unpatients,'" 622.

[392] Geller et al., "Genetic Testing for Susceptibility to Adult-Onset Cancer," 1468.

[393] Ibid. For a discussion of informed consent for predictive genetic testing, see Chapter 7.

[394] For a discussion of genetic exceptionalism and confidentiality, see Chapter 9, page 243.

[395] For a discussion of insurance and employment, see Chapter 10; for a discussion of genetic testing of children, see Chapter 8; for a discussion of genetic research use of tissue samples, see Chapter 7, page 194.

# 5

## Genetic Screening for Adult Health and Reproductive Risks

Genetic screening differs from genetic testing in that it targets populations, not individuals who are perceived to be at higher than normal risk based on family and/or personal medical history.[1] It may be targeted to an entire population or to specific subpopulations, based on known risks for particular groups. Genetic screening includes reproductive screening tests[2] and screening tests that provide the opportunity to prevent or minimize disease in apparently healthy newborns, children, and adults.[3] Screening may be offered in the context of an individual's normal clinical care, for example, during a routine visit to a general practitioner, or it may be organized through a government or community-sponsored program. In some cases, screening tests are designed as initial, and less specific, tests to detect all positive cases in a population (including some who are "false positives") for the purpose of more definitive follow-up testing.[4]

Screening is performed for the following reasons: (1) detection of future disease risk in a person to enable preventive measures; (2) prevention of, or preparation for, the birth of an infant with a serious genetic disorder (reproductive screening); (3) medical or public health research, for example, to determine the incidence of a genetic condition or susceptibility in population groups; (4) identification purposes (forensic screening);[5] and (5) determination of susceptibility to workplace toxic environmental exposures (workplace screening).[6] Many believe that the deciphering of the human genome and the development of new testing technologies, including DNA chips,[7] will permit genetic screening to predict an expanding menu of reproductive and health risks.[8] This chapter

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[1] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 4, 65.

[2] See Chapter 3, page 49; see also page 109, this chapter.

[3] See Chapter 3, page 60; see also page 123, this chapter.

[4] See President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions* (Washington, D.C.: U.S. Government Printing Office, 1983), 2.

[5] See Chapter 3, page 75.

[6] See Chapter 2, page 30; see also N. A. Holtzman, "Medical and Ethical Issues in Genetic Screening — An Academic View," *Environmental Health Perspectives* 104 (1996): 987.

[7] See Chapter 2, page 45.

[8] F. S. Collins, "Shattuck Lecture — Medical and Societal Consequences of the Human Genome Project," *New England Journal of Medicine* 341 (1999): 28; W. Henn, "Genetic Screening with the DNA Chip: a

focuses on reproductive screening, screening of healthy adults to detect carrier status and to determine risks for late-onset disorders, and the packaging of screening tests into "multiplex" panels.[9]

## Genetic Screening: Issues and Concerns

### Special Concerns about Screening

Screening programs test large numbers of individuals for the benefit of a minority.[10] The targeting of predictive testing to a population, as opposed to an individual, may shift the balance of benefits and risks for those who are tested.[11] Persons who seek testing because of family and/or personal history generally perceive themselves to be at high risk and are more likely to be prepared to receive unfavorable results. Those who do not perceive themselves to be at risk generally do not expect unfavorable results and may experience more distress when given such results.[12] One common motivation for predictive testing, reduction of uncertainty,[13] is irrelevant for individuals who do not perceive themselves to be at risk. Another concern about genetic screening is that, although it need not be mandatory, the routine offering of screening tests may pressure individuals to undergo testing to which they would not have consented in a different context.[14] Also, genetic screening tests that target particular groups of people, generally on the basis of racial, ethnic, or geographic origin, may contribute to discrimination and/or stigmatization of members of those groups.[15]

Use of predictive genetic tests to screen healthy populations also raises questions about the required level of a test's predictive value — the chance that someone testing positive will get a disease and that someone testing negative will not get a disease. Even highly specific tests generate higher rates of false positive results when prevalence of the genetic variant tested for in the target population is low (as is the case for screening) versus high (as in clinically indicated testing of at-risk individuals).[16]

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New Pandora's Box?" *Journal of Medical Ethics* 25 (1999): 200; K. C. Smith, "Equivocal Notions of Accuracy and Genetic Screening of the General Population," *Mount Sinai Journal of Medicine* 65 (1998): 178; A. L. Beaudet, "Presidential Address: Making Genomic Medicine a Reality," *American Journal of Human Genetics* 64 (1999): 1; C. Sander, "Genomic Medicine and the Future of Health Care," *Science* 287 (2000): 1977.

[9] Screening of newborns is discussed in Chapter 6.

[10] See H. M. Malm, "Medical Screening and the Value of Early Detection," *Hastings Center Report* 29, no. 1 (1999): 26; S. Stewart-Brown and A. Farmer, "Screening Can Seriously Damage Your Health," *British Medical Journal* 314 (1997): 533.

[11] For a discussion of benefits and risks of reproductive genetic testing, see Chapter 3, page 56. For a discussion of benefits and risks of predictive late-onset testing, see Chapter 3, page 68.

[12] T. M. Marteau and R. T. Croyle, "The New Genetics: Psychological Responses to Genetic Testing," *British Medical Journal* 316 (1998): 693.

[13] See Chapter 3, page 56.

[14] See Chapter 3, page 68.

[15] See page 115, this chapter. See also Chapter 3, page 72; Chapter 4, page 95.

[16] N. A. Holtzman, *Proceed with Caution: Predicting Genetic Risks in the Recombinant DNA Era* (Baltimore: Johns Hopkins University Press, 1989), 93; N. A. Holtzman, "Bringing Genetic Tests into the

In the future, most predictive genetic tests likely will be DNA-based tests. These tests, compared to tests for gene products or metabolites (for example, testing for phenylketonuria (PKU) and Tay-Sachs disease) — which require establishment of an arbitrary baseline positive cutoff level — are subject to lower rates of analytical false positive results.[17] For DNA-based testing to detect risk for single-gene disorders such as Tay-Sachs disease or cystic fibrosis, these types of laboratory-based false positive results will be low. However, predictive genetic tests for susceptibility mutations such as breast cancer susceptibility (BRCA) gene mutations,[18] which generally comprise only one of multiple factors that contribute to development of a disease, present a new complication — all those who test positive for a genetic susceptibility variant will not get the disease.[19]

DNA-based testing also is subject to the generation of false negative results caused by genetic heterogeneity — the test may not encompass all possible mutations within a gene, and mutations in genes other than the one(s) being tested also might increase disease risk.[20]

### Criteria for Screening

Based on the special concerns of population-based screening, several groups have considered basic principles and criteria to guide genetic screening.[21] The National Academy of Sciences Committee for the Study of the Inborn Errors of Metabolism (the NAS Committee) considered issues in newborn and reproductive carrier screening and issued a report in 1975.[22] Since then, other groups have revisited the evolving issues

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Clinic," *Hospital Practice* (January 15, 1998): 107, 125; Holtzman, "Medical and Ethical Issues in Genetic Screening — An Academic View," 987; E. M. Prence, "A Practical Guide for the Validation of Genetic Tests," *Genetic Testing* 3 (1999): 201, 204; American Medical Association Council on Ethical and Judicial Affairs, "Multiplex Genetic Testing," *Hastings Center Report* 28, no. 4 (1998): 15, 16. The number of false positives of a given test is influenced by the overall proportion of true positives and true negatives in a population. For example, for a test with a 10 percent false positive rate, in a high-risk population of 1,000 persons in which 900 are true positives, there will be only 10 false positive results (10 percent of 100). For a lower-risk population of 1,000 in which there are 50 true positives, the number of false positives will be 95 (10 percent of 950).

[17] Holtzman, "Medical and Ethical Issues in Genetic Screening — An Academic View," 987. Screening tests that measure levels of a protein or metabolite, e.g., newborn screening tests for metabolic disorders, establish an arbitrary cutoff level, generally one that will detect all positives at the cost of including false positives. See Chapter 2, page 44.

[18] See Chapter 3, page 63.

[19] For a discussion, see Chapter 3, page 64.

[20] Holtzman, "Medical and Ethical Issues in Genetic Screening," 987–988; Holtzman, "Bringing Genetic Tests into the Clinic," 109. For a discussion of genetic heterogeneity, see Chapter 1, page 14.

[21] See N. Fost, "Ethical Implications of Screening Asymptomatic Individuals," *FASEB Journal* 6 (1992): 2813.

[22] National Academy of Sciences Committee for the Study of Inborn Errors of Metabolism, *Genetic Screening: Programs, Principles and Research* (Washington, D.C.: National Academy of Sciences, 1975). For a discussion of the report, see Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 39–54.

surrounding genetic screening, including a presidential commission (the President's Commission) and the Institute of Medicine's Committee for Assessing Genetic Risks (the IOM Committee), which issued reports in 1983 and 1994, respectively.[23] Professional genetics organizations also have issued guidelines and statements of principle.[24]

In 1983, the President's Commission considered whether genetic screening is different from other medical screening.[25] They concluded that reproductive screening is different in that the information being sought primarily affects future generations.[26] They also concluded that genetic screening to determine a person's need for medical care is not fundamentally different from other types of screening, except for the familial implications of testing results. However, at the time of their report, genetic screening tests to determine risk for late-onset disorders did not exist. Subsequent policy groups have acknowledged special concerns about these tests.[27] For example, a recent national task force concluded that testing healthy people to predict future illness is "the most unique and troublesome aspect of genetic testing."[28]

General criteria for genetic screening tests based on the work of these groups are presented in this section.

### *Value of the Screening Test*

The value of screening for genetic risk for a particular disorder is a function of the seriousness of the disorder, its prevalence in the population, and the availability of preventive interventions.[29] In some cases, for example, reproductive screening of population groups at higher than average risk for having a child with Tay-Sachs disease — a neurodegenerative disease that is uniformly fatal during early childhood — many agree that the value of reproductive screening is high; in other cases, the value of screening may be less clear-cut.[30] Some argue against the routine offering of reproductive screening tests that detect

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[23] President's Commission, *Screening and Counseling for Genetic Conditions.* The commission focused on genetic screening undertaken to permit medical intervention or to provide information, including newborn screening, carrier screening, and prenatal diagnosis; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*.

[24] American College of Medical Genetics, *Principles of Screening: Report of the Subcommittee on Screening of the American College of Medical Genetics Practice Committee*, February 1997, American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/pol-26.htm*, visited December 16, 1998.

[25] President's Commission, *Screening and Counseling for Genetic Conditions*, 3.

[26] Ibid.

[27] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 105–106; National Institutes of Health-U.S. Department of Energy Working Group on the Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, ed. N. A. Holtzman and M. S. Watson (Bethesda: National Institutes of Health, 1997); for a discussion, see Chapter 3, page 62.

[28] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*; see also N. A. Holtzman, "Panel Comment: The Attempt to Pass the Genetic Privacy Act in Maryland," *Journal of Law, Medicine, and Ethics* 23 (1995): 367, 369.

[29] M. R. Natowicz and J. S. Alper, "Genetic Screening: Triumphs, Problems, and Controversies," *Journal of Public Health Policy* 12 (1991): 475, 477.

[30] For a discussion, see Chapter 3, page 59.

disorders of lower or more variable severity.[31] For population screening to detect individuals' personal risks for late-onset diseases, the IOM Committee recommended that population screening be voluntary and confined to "treatable or preventable conditions of relatively high frequency."[32]

### *Purpose of Screening*

The IOM Committee concluded that the primary benefit of screening should be to the individual tested.[33] The President's Commission took the same view, stating that the fundamental value of genetic screening is its ability to "enhance opportunities for individuals to obtain information about their personal health to make autonomous and noncoerced choices based on the information."[34] Others state that when a screening program is established, the purpose of screening, for research or clinical benefit, should be clear, and screening for clinical purposes should be tied to an available intervention.[35] Interventions may include reproductive decision-making, lifestyle changes, and enhanced medical surveillance.

### *Quality of the Screening Test and Its Implementation*

The NAS Committee stated that screening tests should be reliable and accurate, highly sensitive (resulting in few false negative results), and "reasonably specific."[36] Others recommend that population screening tests be appropriately evaluated and offered only when determined to be adequately reliable.[37] The IOM Committee called on professional genetics groups to establish expert panels to review which genetic tests should be offered as a standard of care and under what conditions.[38] Some state that screening programs should not be undertaken in the absence of pilot studies.[39]

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[31] E. R. Hepburn, "Genetic Testing and Early Diagnosis and Intervention: Boon or Burden?" *Journal of Medical Ethics* 22 (1996): 105, 109. See Chapter 3, page 59; see also page 130, this chapter.

[32] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 27.

[33] Ibid., 47.

[34] President's Commission, *Screening and Counseling for Genetic Conditions*, 55.

[35] American College of Medical Genetics, *Principles of Screening*.

[36] National Academy of Sciences, *Genetic Screening: Programs, Principles and Research* (quoted in Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 29).

[37] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 26, 50; Natowicz and Alper, "Genetic Screening: Triumphs, Problems, and Controversies," 477–478; American College of Medical Genetics, *Principles of Screening*; President's Commission, *Screening and Counseling for Genetic Conditions*, 8.

[38] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 50.

[39] Ibid., 49; National Academy of Sciences, *Genetic Screening: Programs, Principles and Research*; President's Commission, *Screening and Counseling for Genetic Conditions*, 8.

### *Whom Should Be Offered Screening*

The IOM Committee stated that there should be equal access to testing for people "at approximate equal risk of having a genetic disorder."[40] In the future, improved and cheaper testing technologies, including DNA chips, may enable general population-based screening for all known variations of a gene at reasonable cost.[41]

## When to Screen

Timing of a screening test is important. The NAS Committee found that if a test is performed for disease prevention and management, the time to offer the test is sometime before the age at which treatment must be started in order to be effective. For testing to assess reproductive risks for single-gene disorders, the time to offer the test is when reproduction is being considered, thereby optimizing reproductive options.[42] The IOM Committee agreed, rejecting the claim that screening should be delayed until pregnancy because most women will not come in for care until they are pregnant.[43]

### *How to Screen*

Testing must be voluntary and accompanied by adequate pretest education and informed consent.[44] The IOM Committee stated that the standard should be to "offer" a screening test.[45] Appropriate posttest counseling and follow-up evaluation are also essential.[46] Screening programs also must have effective processes for storing and processing test results.[47] Some stipulate that all genetic screening test results must be confidential and acknowledge concerns for potential discrimination by insurers or employers based on test results.[48]

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[40] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 47. The IOM Committee disagrees with the earlier NAS Committee that testing should be offered to everyone because singling out subpopulations raises the potential for stigmatizing groups.

[41] See, e.g., Henn, "Genetic Screening with the DNA Chip," 200. For a discussion of DNA chips, see Chapter 2, page 45.

[42] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 51.

[43] Ibid., 52.

[44] Ibid., 49–50; Natowicz and Alper, "Genetic Screening: Triumphs, Problems, and Controversies," 478; American College of Medical Genetics, *Principles of Screening*. The American College of Medical Genetics states that there should be a defined population for screening, e.g., "a specific ethnic group for a disorder with increased frequency in that group."

[45] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 51. The committee's use of the word "offer" was intended to distinguish notifying a patient about an available test and its purpose from directively recommending a test.

[46] Ibid.; 49, National Academy of Sciences, *Genetic Screening: Programs, Principles and Research*; American College of Medical Genetics, *Principles of Screening*.

[47] Natowicz and Alper, "Genetic Screening: Triumphs, Problems, and Controversies," 478–479.

[48] American College of Medical Genetics, *Principles of Screening*, President's Commission, *Screening and Counseling for Genetic Conditions*, 6. For a discussion of discrimination, see Chapter 9.

### *Reasonable Screening Costs*

Screening programs must be economically feasible, conferring significant benefit to enough individuals to justify the expenses of screening.[49] However, the President's Commission and the IOM Committee emphasized the limits of cost-effectiveness analysis for genetic testing and screening, where indirect costs and benefits, including psychological costs and benefits, are difficult to measure.[50] They also pointed out that for screening, simple aggregation of "gains and losses across all the individuals affected omits considerations of equity and fairness."[51] They both recommended that cost-benefit analysis be used within an ethical framework, rather than as a method of avoiding difficult ethical judgments.[52] In the future, new testing technologies such as DNA chips and tandem mass spectrometry may render cost issues less central because of their ability to test for multiple genetic variants in single assays, probably at decreasing costs.[53]

The IOM Committee noted that while cost-benefit analysis may play a part in allocational decision-making for screening programs, the reduction of health costs cannot justify compulsory screening.[54] They expressed concerns about the implications of cost-benefit analysis for predictive genetic screening when uncertainties about test results may exist and effective treatments are often unavailable.[55] They and others also note the particularly grave consequence that could result from using monetary costs and benefits to justify reproductive screening.[56]

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[49] Natowicz and Alper, "Genetic Screening: Triumphs, Problems, and Controversies," 478; for a discussion of cost analysis for policies regarding health and standards of health care delivery, see D. C. Wertz, "Statement on Cost-Effectiveness and Cost-Benefit Analysis from the New England Regional Genetics Group," *The Gene Letter* (August 1997), website: *http://www.geneletter.org*, visited December 1, 1997.

[50] President's Commission, *Screening and Counseling for Genetic Conditions*, 84; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 304–305.

[51] President's Commission, *Screening and Counseling for Genetic Conditions*, 84.

[52] Ibid.

[53] See, e.g., Collins, "Medical and Societal Consequences of the Human Genome Project," 28; H. L. Levy, "Newborn Screening for Tandem Mass Spectrometry: A New Era," *Clinical Chemistry* 44 (1998): 2401.

[54] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 6, 8, 47. See also Chapter 4, page 95.

[55] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 53.

[56] Ibid.; see also J. R. Botkin, "Prenatal Screening: Professional Standards and the Limits of Parental Choice," *Obstetrics and Gynecology* 75 (1990): 875, 878; D. T. Morris, "Cost Containment and Reproductive Autonomy: Prenatal Genetic Screening and the American Health Security Act of 1993," *American Journal of Law and Medicine* 20 (1994): 295, 302–303.

## Reproductive Screening Tests

### Prenatal Screening Tests

#### *Maternal Serum Screening*

Maternal serum screening is a noninvasive testing method performed on a blood sample obtained from a woman early in pregnancy to determine fetal risk for neural tube defects,[57] Down syndrome, and trisomy 18.[58] Maternal serum screening is an example of a preliminary screening test that detects, from a larger population, a smaller group of high-risk women who require further testing.[59] For neural tube defects, the test detects women with a 1 in 20 risk, versus a 1 in 1,000 risk for the general population; it detects about 85 percent of affected fetuses.[60] Screening detects 60 percent of fetuses with Down syndrome, with a 5 percent false positive rate.[61]

The original test, for a single maternal serum marker, alpha-fetoprotein, indicated pregnancies at risk for neural tube defects. The screening test was adopted in the United Kingdom in the late 1970s; its approval and implementation in the United States occurred in the mid-1980s, following some debate regarding the potential harms of screening.[62] The American College of Obstetricians and Gynecologists (ACOG) supported the screening test as a standard of care for all pregnant women who would be under age thirty-five at the time of delivery, and they issued a professional liability "alert" advising obstetricians about professional liability implications of not offering, and documenting the offering, of the test.[63]

When researchers later found that analysis of serum alpha-fetoprotein and two additional serum components could provide risk information about Down syndrome and trisomy 18, "triple marker" screening was rapidly introduced and endorsed by the

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[57] For a discussion of neural tube defects, see March of Dimes, *Fact Sheet: Spina Bifida*, March of Dimes website: *http://www.modimes.org*, visited August 18, 1999.

[58] American College of Obstetricians and Gynecologists, *Educational Bulletin: Maternal Serum Screening*, no. 228, September 1996. For a discussion, see Chapter 3, page 52. Trisomy 18, like Down syndrome, is caused by the inheritance of an extra copy of a chromosome, in this case, chromosome 18.

[59] See Chapter 3, page 52. This test does not meet this report's definition of a genetic test. The follow-up tests include ultrasonography and invasive fetal cell testing. The tests are more specific and more costly.

[60] American College of Obstetricians and Gynecologists, *Educational Bulletin: Maternal Serum Screening*, 3.

[61] Ibid., 6. The incidence of live births with Down syndrome is about 1 in 800.

[62] The test was approved by the Food and Drug Administration in 1983. See Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 79. For a discussion of test implementation in the United States, see N. Press and C. H. Browner, "Risk, Autonomy, and Responsibility: Informed Consent for Prenatal Testing," *Hastings Center Report* 25, no. 3 (suppl.): S9; see also H. Markel, "Scientific Advances and Social Risks: Historical Perspectives of Genetic Screening Programs for Sickle Cell Disease, Tay-Sachs Disease, Neural Tube Defects and Down Syndrome," in NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 161, 167–169.

[63] American College of Obstetricians and Gynecologists, *Professional Liability Implications of AFP Testing* (Liability Alert), May 1985. For a discussion, see Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 79.

professional genetics societies.[64] Triple marker screening has not, however, received approval by the Food and Drug Administration.[65] One state, California, mandates that maternal serum screening be offered to all pregnant women.[66]

Some commentators continue to express concern that the driving force behind professional endorsement of maternal serum screening was not the benefit of the woman tested but the protection of physicians from litigation for "wrongful births."[67] Others suggest that adoption of screening without discussion of ethical, legal, and social issues was inappropriate[68] and cite evidence that physicians sometimes pressure women to be screened and do not obtain meaningful consent.[69] The IOM Committee acknowledged that maternal serum marker screening is sometimes performed without adequate pretest education and consent, resulting in anxiety among women who have no reason to consider their fetuses to be at risk for a genetic disorder.[70] It affirmed, however, that screening should be offered as voluntary and that patients must be informed that a positive test result may indicate further evaluation that may include amniocentesis.[71] It also emphasized the importance of counseling services to those who test positive in more specific follow-up testing.

### *Invasive Fetal Screening Tests*

The genetic testing of fetal cells and amniotic fluid obtained by amniocentesis or of fetal cells by chorionic villus sampling is offered as a specific diagnostic follow-up test to women testing positive for maternal serum markers and to women at known familial risk for a genetic disorder.[72] It also is offered as the standard of care as a screening test to all

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[64] J. E. Haddow et al., "Prenatal Screening for Down Syndrome with the Use of Maternal Serum Markers," *New England Journal of Medicine* 327 (1992): 588; American College of Obstetricians and Gynecologists, *Committee Opinion: Down Syndrome Screening*, August 1994.

[65] Markel, "Scientific Advances and Social Risks," 169.

[66] R. Steinbrook, "In California, Voluntary Mass Prenatal Screening," *Hastings Center Report* 26, no. 5 (1996): 5; Press and Browner, "Risk, Autonomy, and Responsibility," S11. In mid-1995, the program implemented triple marker screening. G. Cunningham and G. Tompinson, "Cost and Effectiveness of the California Triple Marker Prenatal Screening Program," *Genetics in Medicine* 1 (1999): 199, 201.

[67] Press and Browner, "Risk, Autonomy, and Responsibility," S11; see also L. Wingerson, *Unnatural Selection: The Promise and Power of Human Genome Research* (New York: Bantam Books, 1998), 30. A wrongful birth lawsuit may be initiated by parents against a physician following the birth of a child affected by a congenital disorder that might have been detected prenatally, had the physician offered prenatal testing. See L. B. Andrews, "Torts and the Double Helix: Malpractice Liability for Failure to Warn of Genetic Risks," *Houston Law Review* 29 (1992): 149.

[68] Press and Browner, "Risk, Autonomy, and Responsibility," S9–S10.

[69] N. A. Press and C. H. Browner, "'Collective Fictions': Similarities in Reasons for Accepting Maternal Serum Alpha-Fetoprotein Screening among Women of Diverse Ethnic and Social Backgrounds," *Fetal Diagnosis and Therapy* 8 (suppl. 1) (1993): 97, 101–102. In a survey of forty cases, the average pretest discussion between provider and patient was two minutes. In only two of forty cases, providers mentioned the possibility of "pregnancy termination" or "abortion."

[70] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 103–104.

[71] Ibid., 104–105; American College of Obstetricians and Gynecologists, *Educational Bulletin: Maternal Serum Screening*.

[72] See Chapter 3, page 51.

pregnant women who will be age thirty-five or older at the projected date of birth, based on the increased fetal risk for chromosomal abnormalities for women of advanced maternal age.[73] At maternal age thirty-five, the risk for an affected fetus equals the risk for testing-induced miscarriage, approximately 1 in 200.[74] This test, unlike maternal serum screening, is a highly specific diagnostic test, although in some cases it also may detect results of uncertain clinical significance.[75]

The IOM Committee stated that in circumstances of increased fetal risk for genetic disorders, including advanced maternal age, offering prenatal genetic diagnosis should be the standard of care.[76] They also stated that adequate counseling and education should be the standard of care, even if less invasive techniques, such as maternal fetal cell testing (using fetal cells present in a routine blood sample obtained from a pregnant woman), become available.[77] They recommended that third-party payers should reimburse for appropriate prenatal diagnostic testing but that test results should not be disclosed to payers.[78]

### Carrier Screening Tests

Carrier testing aims to identify healthy individuals who are at risk for bearing children with genetic disorders.[79] It may be performed as a preconception test for individuals considering marriage or pregnancy.[80] It also may be performed as a prenatal test, in which both parents can be tested to determine whether or not an already-conceived fetus is at risk; in this case, it is called a prenatal carrier test. Carrier testing may provide expanded reproductive options for the individuals or couples tested.[81]

Carrier testing may be targeted to individuals based on family history of a recessive single-gene disorder such as cystic fibrosis or Duchenne muscular dystrophy. Carrier testing also is performed as a population screening test targeted to individuals of a particular racial, ethnic, or geographic population that is known to be at increased risk for a particular autosomal recessive disorder.[82]

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[73] American College of Obstetricians and Gynecologists, *Technical Bulletin: Antenatal Diagnosis of Genetic Disorders*, Number 108, September 1987, 1; American Academy of Pediatrics and American College of Obstetricians and Gynecologists, *Guidelines for Perinatal Care*, 3d ed., 1992, 59; American College of Medical Genetics, *Statement on Multiple Marker Screening in Pregnant Women*, 1996, American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/pol-18.htm*, visited July 22, 1998.

[74] See Chapter 3, page 57.

[75] See Chapter 3, page 58.

[76] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 103.

[77] Ibid.; for a discussion of maternal fetal cell testing, see Chapter 3, page 52.

[78] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 105.

[79] For a discussion, see Chapter 3, page 50.

[80] For discussion of carrier screening programs targeted to unmarried young adults and adolescents, see page 121, this chapter. For a discussion of genetic testing of minors, see Chapter 8.

[81] For a discussion, see Chapter 3, page 56.

[82] Population-based genetic risks are caused by "founder mutations." For a discussion, see Chapter 3, page 63.

### *A Successful Screening Model: Tay-Sachs Disease*

One in 30 Ashkenazi Jewish Americans, versus 1 in 300 other Americans, are carriers for Tay-Sachs disease, a neurodegenerative disease that is fatal within the first several years of life.[83] Before carrier screening for Tay-Sachs disease started in the early 1970s, approximately 1 in 4,000 newborns of Ashkenazi Jewish parents were affected.[84]

Tay-Sachs carrier screening provides a prototypical model[85] for carrier screening because of the following factors: (1) the severity of the disease, a uniformly fatal, "devastating" disorder; [86] (2) the fact that the disease affects 100 percent of infants who inherit two mutant gene copies; (3) the absence of any effective medical treatment options; (4) the ability to target an identifiable and motivated high-risk group for screening; (5) the availability of a relatively simple, clinically valid, and inexpensive carrier test; and (6) the availability of an effective prenatal diagnostic test for identified carrier couples.

In the 1970s, Tay-Sachs screening programs were initiated at the community level, and the "unrelenting vigilance" of the community and religious representatives and physicians who planned and implemented the programs was critical to their success.[87] Programs provided education and incorporated informed consent, steps to ensure confidentiality, and pretest and posttest counseling. Most programs targeted young married couples who were contemplating pregnancy, although others reached more broadly for all unmarried eighteen-year-olds. Another factor in the program's success was the use of pilot studies to test the validity and reliability of the enzyme-based screening test.[88]

Tay-Sachs carrier screening, coupled with effective prenatal diagnosis, has resulted in a 95 percent reduction in the number of new Tay-Sachs births.[89] By 1993,

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[83] American College of Gynecologists and Obstetricians, *Screening for Tay-Sachs Disease*, Committee Opinion 162, November 1995. Persons of French Canadian and Cajun populations also have a greater carrier frequency than the general population.

[84] Ibid. Frequency of autosomal recessive disorders can be calculated as the chance of two asymptomatic carriers meeting and reproducing and the chance that any one child will inherit an affected allele from each parent (one in four). Thus, in the Ashkenazi Jewish community, the chance of an affected child is calculated as (1/30 x 1/30) (1/4). Approximately 1 in 360,000 newborns of the general population is affected.

[85] For a discussion, see Natowicz and Alper, "Genetic Screening: Triumphs, Problems, and Controversies," 480–481; see also Markel, "Scientific Advances and Social Risks," 165–167; President's Commission, *Screening and Counseling for Genetic Conditions*, 19.

[86] Natowicz and Alper, "Genetic Screening: Triumphs, Problems, and Controversies," 481.

[87] Markel, "Scientific Advances and Social Risks," 167; see also President's Commission, *Screening and Counseling for Genetic Conditions*, 13.

[88] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 42.

[89] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 296.

36,000 carriers and 1,056 carrier couples had been detected worldwide.[90] Thousands of healthy infants have been born to at-risk couples, many of whom may not have initiated pregnancies in the absence of a reliable genetic prenatal test.[91] Screening continues today, generally integrated into clinical health care[92] and facilitated by the availability of a DNA-based test that detects the three most common gene mutations that cause Tay-Sachs disease in the Ashkenazi Jewish population, for an overall sensitivity of 98 percent.[93]

### *A Problematic Screening Model: Sickle Cell Disease*

A carrier screening program for sickle cell disease, also implemented in the early 1970s, exemplifies the harms that may result when a screening program lacks clearly defined goals and is poorly planned and implemented. Sickle cell disease is a serious autosomal recessive blood disorder that is frequent in the African American community; in this community, the carrier rate is 1 in 12, and the incidence of newborns with the disease is about 1 in 600.[94]

The disease is caused by inheritance of two mutant copies of the gene that codes for the beta globin protein, a component of hemoglobin contained in red blood cells. The abnormal hemoglobin protein that results causes red cells to deform, or "sickle," resulting in episodic circulation blockages and severe pain.[95] The disorder also increases risk for potentially lethal bacterial infections and causes long-term organ damage. The severity of the disorder and the lifespan of affected individuals can vary significantly.

Many sickle cell carrier screening programs of the 1970s, unlike Tay-Sachs disease carrier screening programs, were initiated and sponsored by government.[96] In 1971, President Richard Nixon pledged increased federal support for treatment and research of sickle cell anemia, and Senate hearings resulted in establishment of a national sickle cell anemia program.[97] Seventeen states, including New York State, enacted screening laws, some of them mandatory.[98] Laws exclusively targeted African

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[90] M. Kabach, "Tay-Sachs Disease," 2309; see also Chapter 3, page 56.
[91] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 43.
[92] The American College of Obstetricians and Gynecologists recommends that carrier testing for Tay-Sachs disease be offered, ideally before pregnancy, to both members of couples of Ashkenazi Jewish descent. American College of Obstetricians and Gynecologists Committee on Genetics, *Screening for Tay-Sachs Disease*, ACOG Committee Statement no. 162, November 1995.
[93] Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 296.
[94] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 41.
[95] For a discussion of the disease, see March of Dimes, *Fact Sheet: Sickle Cell Disease*, March of Dimes website: *http://www.modimes.org*, visited August 18, 1999; Gelehrter, Collins, and Ginsburg, *Principles of Medical Genetics*, 98.
[96] President's Commission, *Screening and Counseling for Genetic Conditions*, 17–22.
[97] H. Markel, "The Stigma of Disease: Implications of Genetic Screening," *American Journal of Medicine* 93 (1992): 209, 212–213. A 1972 New York State law requires testing of applicants for marriage licenses for the purpose of "discovering the existence of sickle cell anemia" to persons "not of the Caucasian, Indian or Oriental race." N.Y.S. C.L.S. Dom Rel § 13-aa (McKinney 1999).
[98] L. B. Andrews, "Sickle Cell Screening Laws and Regulations," in *State Laws and Regulations Governing Newborn Screening* (Chicago: American Bar Foundation, 1985): 147.

Americans, despite similar risks of related conditions in other ethnic groups (e.g., thalassemia in people of Mediterranean heritage).[99]

Screening programs "evolved in a rapid, haphazard, often poorly planned fashion, generated in large measure by public clamor and political pressure."[100] Physicians were not sufficiently knowledgeable and education efforts were inadequate.[101] There was no effective prenatal diagnostic test available for couples in which both individuals were identified as carriers.[102] Also, unlike for the uniformly fatal Tay-Sachs disease, avoiding the birth of an affected child "was less widely regarded in the relevant population groups as obviously desirable."[103] The timing of screening was questionable, targeting school-aged children as well as young adults of marriage age.[104]

Another major problem was that the testing methods lacked adequate analytical validity. The initial laboratory test did not distinguish between the individuals who had inherited the autosomal recessive disease and the much higher number of individuals who were healthy carriers of a single sickle cell gene mutation.[105] The National Sickle Cell Anemia Control Act itself failed to make the distinction between disease and carrier status, incorrectly stating that "sickle cell anemia is a debilitating, inheritable disease that affects approximately two million Americans." In fact, there were approximately two million carriers, but only 50,000 persons were affected by the disease.[106]

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[99] See Markel, "Scientific Advances and Social Risks," 163.

[100] National Academy of Sciences, *Genetic Screening: Programs, Principles and Research*, 117 (quoted in President's Commission, *Screening and Counseling for Genetic Conditions*, 21). See also D. Wertz, "Sickle Cell Testing: Past and Present," *The Gene Letter* (July 1996), website: *http://www.geneletter.org*, visited January 29, 1998.

[101] Markel, "The Stigma of Disease," 213. For example, one 1974 survey of 160 physicians found that one in seven believed carrier status to be a disease.

[102] Until 1978, the only prenatal test available required a fetal blood sample, posing high risk to the fetus. Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 42.

[103] President's Commission, *Genetic Screening and Counseling*, 22.

[104] N. A. Holtzman, *Proceed with Caution*, 219. Newborn hemoglobinopathy screening programs began about 1976. See R. Murray, "The Ethics of Predictive Genetic Screening: Are the Benefits Worth the Risks?" in *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp (Tuskegee, AL: Tuskegee University, 1997), 139, 145.

[105] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 41; Wertz, "Sickle Cell Testing: Past and Present."

[106] Holtzman, *Proceed with Caution*, 219 (citing Phillip Reilly, M.D., J.D.). See also Murray, "The Ethics of Predictive Genetic Screening," 143. Murray states, "People who have the carrier trait are generally quite healthy. There is some evidence that a very small minority of individuals who are carriers of the sickle cell gene might be at risk for certain physical problems under extreme conditions. But these are rare, and there is still no definitive proof that that the presence of the sickle cell trait [carrier status] is responsible for these abnormalities." Ibid. Sickle cell carrier status is sometimes referred to as "sickle cell trait," likely contributing to the misperception that carriers are affected.

Psychosocial harms resulted for individuals who were carriers but mistakenly believed they had the disease. For example, in a Chicago screening program sponsored by the political activist group the Black Panthers, about 10 percent of parents were reportedly misinformed that their children had inherited the disease and would likely die by age twenty.[107] Discrimination also resulted. In at least five states, marriage licenses and/or school attendance were denied to those who refused testing.[108] Adults faced discrimination in health and life insurance and in employment.[109] In response to an erroneous medical report that claimed shortened longevity for sickle cell carriers, over a quarter of life insurance companies raised their premiums for carriers by as much as 25 percent.[110] Based on the unclear purpose of screening, the absence of a prenatal diagnostic test, and the targeting of African Americans, some perceived screening as a form of anti-black eugenics or a step toward genocide.[111]

Government efforts to redress these mistakes eventually helped promote high-quality carrier and disease screening programs.[112] By the early 1980s, an effective and reliable prenatal diagnostic test for sickle cell disease was available.[113] Most state screening laws for sickle cell screening, with the exception of screening in newborn programs, have been revised or abolished.[114] For reproductive screening, ACOG recommends that obstetricians attempt to identify couples at increased risk for having offspring with sickle cell disease or related blood disorders (hemoglobinopathies) such as thalassemia.[115]

### *Cystic Fibrosis Screening Debate*

Almost thirty years later, a new debate has developed regarding the appropriateness of population-based carrier screening for another autosomal recessive disorder, cystic fibrosis. Cystic fibrosis is the most frequent autosomal recessive disorder among Caucasians in the United States, with a carrier incidence of 1 in 29 and a disease incidence of 1 in 3,300.[116] It is a disease with variable presentation and course, generally

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[107] Wertz, "Sickle Cell Testing: Past and Present."
[108] Holtzman, *Proceed with Caution*, 219.
[109] Markel, "The Stigma of Disease," 213; see also Chapter 10, page 281.
[110] Ibid.; J. E. Bowman, "Genetics and the Law: The Ethical, Legal and Social Implications of Genetic Technology and Biomedical Ethics: The Road to Eugenics," University of Chicago Law School Roundtable 491, 1996, 71; Murray, "The Ethics of Predictive Genetic Screening," 146.
[111] Murray, "The Ethics of Predictive Genetic Screening," 145; D. J. Kevles, *In the Name of Eugenics: Genetics and the Uses of Human Heredity*, 2d ed. (Cambridge, MA: Harvard University Press, 1997), 278.
[112] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 42.
[113] Wertz, "Sickle Cell Testing: Past and Present."
[114] Andrews, "Sickle Cell Screening Laws and Regulations."
[115] American College of Obstetricians and Gynecologists, *Genetic Screening for Hemoglobinopathies*, Committee Opinion no. 168, February 1996. Also, in 1983, the establishment of penicillin prophylaxis as a useful treatment to prevent morbidity and mortality of children with the disease provided a rational basis for sickle cell disease screening of newborns. See National Institutes of Health Consensus Conference, "Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies," *Journal of the American Medical Association* 258 (1987): 1205. See also Chapter 6, page 144.
[116] National Institutes of Health, *NIH Consensus Statement: Genetic Testing for Cystic Fibrosis* 15 (April 14–16, 1997), 8, National Institutes of Health website: *http:// consensus.nih.gov*, visited August 27, 1999.

characterized by pulmonary (lung), and sometimes gastrointestinal, disease.[117] In 1995, median survival of those diagnosed with cystic fibrosis was 30.1 years, but in rare cases, affected individuals have a normal lifespan.[118]

In 1989, researchers discovered the gene that, when mutated, leads to cystic fibrosis.[119] The gene, called CFTR, is very large, containing over 6,000 DNA bases that encode for a protein that functions in the transport of fluids and salts across cell membranes.[120] Researchers have discovered hundreds of different clinically relevant mutations at key bases in this gene that can prevent the production of functional protein. In individuals who inherit two mutant CFTR gene variants and cannot make normal CFTR protein, tissue secretions in the lungs and gastrointestinal organs are abnormally viscous, causing emphysema and gastrointestinal malabsorption.

Discovery of the gene and mutations associated with cystic fibrosis allowed both carrier and prenatal testing for individuals at high reproductive risk because of family history. The high prevalence of CFTR gene mutations, the seriousness of the disorder, and the availability of sensitive and accurate DNA-based testing methods also prompted consideration of more widespread carrier screening. In April 1997, a National Institutes of Health (NIH) Consensus Development Conference was convened to assess the optimal practices for testing for cystic fibrosis carriers.[121] In the resulting consensus statement, the panel recommended that cystic fibrosis carrier testing should be offered "to the prenatal population and couples currently planning a pregnancy, particularly those in high risk populations."[122] Several commentators noted that this recommendation would likely lead to the offering of cystic fibrosis carrier testing to all pregnant women as the standard

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[117] For a review of the genetics and clinical aspects of cystic fibrosis, see T. Brown and E. Langfelder Schwind, "Update and Review: Cystic Fibrosis," *Journal of Genetic Counseling* 8 (1999): 137; P. T. Rowley, S. Loader, and J. C. Levenkron, "Cystic Fibrosis Carrier Population Screening: A Review," *Genetic Testing* 1 (1997): 53. For general information about the disease, testing, and treatments, see the Cystic Fibrosis Foundation website: *http://cff.org*, visited May 17, 2000.

[118] National Institutes of Health, *NIH Consensus Statement*, 5.

[119] J. R. Riordan et al., "Identification of the Cystic Fibrosis Gene: Cloning and Characterization of the Complementary DNA," *Science* 245 (1989): 1066; J. M. Rommens et al., "Identification of the Cystic Fibrosis Gene: Chromosome Walking and Jumping," *Science* 245 (1989): 1059.

[120] Rommens et al., "Identification of the Cystic Fibrosis Gene," 1059. The CFTR (cystic fibrosis transmembrane regulator) gene contains twenty-six exons; including the intron sequences that "interrupt" the coding sequence, the gene spans about 250,000 DNA bases. For a discussion of gene exons and introns, see Chapter 1, page 9.

[121] National Institutes of Health, *NIH Consensus Statement*. The panel was one of a series of consensus development panels established in 1977 as a "science court" mechanism to "resolve controversial topics in medicine and public health in an unbiased, impartial manner." See "CF Genetic-Testing Panel Emphasizes Education," *Human Genome News*, January 1998, 13.

[122] National Institutes of Health, *NIH Consensus Statement*, 16.

of care, based on physician fear of litigation.[123] In fact, a survey of clinical genetics centers in New York, Puerto Rico, and the Virgin Islands showed that about half of centers that offered cystic fibrosis carrier screening altered their screening policies following the NIH consensus statement, either by offering screening to patients "at higher risk ethnicities" or by extending screening to all patients.[124]

In October 1997, an NIH Workshop was convened to consider implementation of the consensus recommendations. Workshop participants concluded that several issues must be resolved before the offering of testing to all pregnant women becomes the standard of care, and that resolution would require a minimum of eighteen to thirty-six months.[125] The American College of Medical Genetics (ACMG) and ACOG reached similar conclusions.[126] Issues include adequacy of education and counseling systems and the reliability of the screening test for different racial and ethnic groups. Following the NIH Workshop, a joint steering committee of the NIH, ACOG, and ACMG was convened to implement its recommendations.[127]

The scientific, medical, and social components of such a screening initiative are examined in this section, based on the recommended principles and guidelines for genetic screening programs.[128]

*Value of the Screening Test*

Cystic fibrosis is a serious disorder but, unlike Tay-Sachs disease, symptoms, disease severity, and lifespan are variable. Affected individuals display mild to severe symptoms, and, although there is no cure, disease management interventions have greatly increased life expectancy.[129] For adults with cystic fibrosis, over one-third are married or live with companions and over three-quarters are employed, students, or homemakers.[130]

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[123] D. C. Wertz, "NIH Recommends Carrier Testing for Pregnant Women," *The Gene Letter*, May 1997, website: *http//www.geneletter.org*, visited August 30, 1999; J. Schmidtke, "A Commentary on the NIH Consensus Development Statement 'Genetic Testing for Cystic Fibrosis,'" *Community Genetics* 1 (1998): 53, 54.

[124] E. Langfelder Schwind et al., "Cystic Fibrosis Carrier Screening Practices in an Ethnically Diverse Region: Experience of the Genetic Network of the Empire State, Puerto Rico, and the U.S. Virgin Islands," *Genetic Testing* 3 (1999): 215. Patient ethnicity bases of the centers was a significant factor in policy, however, with centers serving "lower-risk" ethnic populations less likely to offer testing at all, and some centers offering testing to only limited groups. Ibid., 217.

[125] M. T. Mennuti, E. Thompson, and N. Press, "Screening for Cystic Fibrosis Carrier State," *Obstetrics and Gynecology* 93 (1999): 456, 461.

[126] American College of Medical Genetics, *Statement on Genetic Testing for Cystic Fibrosis*, October 28, 1997, American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/pol-32.htm*, visited September 30, 1998; "ACOG Statement on Cystic Fibrosis Statement," September 13, 1997, *ACOG Today* 42 (May/June 1998): 7.

[127] See M. T. Menutti, "Offering CF Carrier Screening: Who Set the Goal, and What Is the Goal?" *Genetics in Medicine* 1 (1999): 125.

[128] See page 104, this chapter.

[129] For a discussion of clinical management procedures and investigational stage treatments, see Brown and Langfelder Schwind, "Update and Review: Cystic Fibrosis," 139–142.

[130] Ibid.

The NIH consensus statement acknowledges these factors but considers the disease sufficiently serious to warrant general screening, provided adequate education and counseling occur. Others agree, including one professional conference report that noted that "nearly all affected individuals have substantial multi-system disease."[131]

The NIH consensus panel concluded that the incidence of cystic fibrosis in American populations justifies screening. Disease incidence is about 1 in 3,300 for Caucasians, 1 in 9,500 for Hispanics, 1 in 15,300 in African Americans, and 1 in 32,000 in Asian Americans.[132]

*Purpose of Screening*

The NIH consensus statement holds that the aim of testing is to provide information for informed decision-making.[133] Carrier testing expands reproductive options, allowing DNA-based testing by prenatal diagnosis or pre-implantation testing of embryos. In several studies, the majority of at-risk couples detected by carrier screening chose prenatal diagnosis.[134]

*Predictive Value of the Screening Test*

DNA-based testing is highly accurate, but current testing technology cannot detect all clinically significant mutations because of the large size and complexity of the CFTR gene. Although over 800 different CFTR gene mutations have been identified, DNA-based testing detects less than 90 percent of mutations in the general Caucasian population and only 30 percent of mutations in the Asian American population.[135] About two dozen mutations are common worldwide, but many others are rare, and particular mutations are more common in individuals of different ethnic backgrounds. A screening test that scores for a limited panel of mutations, therefore, will generate different rates of false negatives in different populations.

Even for these identified mutations, the clinical impact on an individual based on the inherited gene variants may be difficult to predict. While particular mutations can be

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[131] J. E. Haddow et al., "Issues in Implementing Prenatal Screening for Cystic Fibrosis: Results of a Working Conference," *Genetics in Medicine* 1 (1999): 129.

[132] National Institutes of Health, *NIH Consensus Statement*, 7–8. The incidence for native Africans and Asians is lower, less than 1 in 50,000.

[133] National Institutes of Health, *NIH Consensus Statement*, 18.

[134] Rowley, Loader, and Levenkron, "Cystic Fibrosis Carrier Population Screening," 53; D. J. Brock, "Prenatal Screening for Cystic Fibrosis: 5 Years' Experience Reviewed," *The Lancet* 347 (1996): 148. A lower rate of uptake was reported for a study involving couples with a previously affected child. See Brown and Langfelder Schwind, "Update and Review: Cystic Fibrosis,"149.

[135] See Brown and Langfelder Schwind, "Update and Review: Cystic Fibrosis," 143; National Institutes of Health, *NIH Consensus Statement*, 8.

strongly correlated with pancreatic impairment, the impact of particular mutations on lung disease, the major factor affecting quality of life and longevity for a cystic fibrosis patient, is more difficult. There also is evidence that disease pathology is significantly affected by other, not fully identified, environmental and genetic factors.[136]

The high number of detectable CFTR gene mutations, uncertainty about how many of these mutations affect the disease process, and the different incidence of mutations in different populations can lead to dilemmas about which mutations to test for. There is not yet a standard of care for which mutations should be surveyed, and different testing laboratories use different methods and different mutation testing panels.[137]

*Whom Should Be Offered Screening*

Based on differences in test sensitivity for different populations, some disagree with the NIH consensus recommendation that testing be offered to pregnant women of all ethnic and racial backgrounds.[138] Questions also remain about whether testing should be offered only to those groups at some threshold risk for disease. For example, one professional group suggested that screening should be offered to any population with a carrier rate of one in thirty-five or greater.[139]

*When to Screen*

The NIH consensus panel considered research that showed that, in the general population, interest in testing for cystic fibrosis carrier status occurs primarily among pregnant women.[140] Reasons for interest among pregnant women are diverse. Some are interested in prenatal testing and possible pregnancy termination, whereas others only wish to know their carrier status, perhaps to prepare for the possibility of an affected child.[141] One studied also showed that obstetrician-gynecologists offered screening exclusively to pregnant women, apparently for logistical reasons.[142]

The NIH consensus panel's recommendation to offer the test to pregnant women is counter to recommendations of the NAS and IOM Committees, which favored preconception testing.[143] The NIH Workshop agreed with the consensus statement that

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[136] National Institutes of Health, *NIH Consensus Statement*, 9. Brown and Langfelder Schwind, "Update and Review: Cystic Fibrosis," 147.

[137] Brown and Langfelder Schwind, "Update and Review: Cystic Fibrosis," 152; see also W. W. Grody et al., "Diversity of Cystic Fibrosis Mutation-Screening Practices," *American Journal of Human Genetics* 62 (1998): 1252.

[138] Mennuti, Thompson, and Press, "Screening for Cystic Fibrosis Carrier State," 458; American College of Medical Genetics, "Statement on Genetic Testing for Cystic Fibrosis."

[139] Haddow et al., "Issues in Implementing Prenatal Screening for Cystic Fibrosis," 132.

[140] National Institutes of Health, *NIH Consensus Statement*, 12. See also "ELSI's Cystic Fibrosis Experiment," *Science* 274 (1996): 489.

[141] National Institutes of Health, *NIH Consensus Statement*, 12.

[142] S. Loader et al., "Cystic Fibrosis Carrier Population Screening in the Primary Care Setting," *American Journal of Human Genetics* 59 (1996): 234.

[143] See page 108, this chapter.

while preconception screening is more desirable, data show a lack of interest in screening by the nonpregnant population.[144]

*How to Screen*

The NIH consensus statement declares that screening efforts must be accompanied by educational programs targeted to health care professionals and the general public, that genetic counseling services must be available and accurate, and that every attempt should be made to protect "individual rights, and genetic and medical privacy rights."[145] The panel cites concerns among the public that disclosure of test results might affect family relationships or may lead to discrimination by employers or health insurers.[146] It stipulates that it is essential that screening be phased in over time to ensure appropriate education and counseling.

Commentators contend that the complications of CFTR gene testing, the different mutation patterns in different populations, and the evolving data about the clinical significance of particular mutations are beyond the scope of most practicing primary care and prenatal providers.[147] These concerns are supported by survey data that show that many obstetrician-gynecologists could not correctly answer multiple-choice questions about CFTR gene mutations and carrier frequencies in different populations.[148]

*Reasonable Screening Costs*

The NIH consensus panel stated that 1997 testing costs ranged from $50 to $150 per test, each test including a panel of six to seventy-two mutations; they also predicted that testing costs will continue to decline.[149] The panel noted that counseling and educational costs also must be taken into account. The consensus report cites studies that estimate medical cost savings based on averted cystic fibrosis pregnancies.[150] One

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[144] Mennutti, Thompson, and Press, "Screening for Cystic Fibrosis Carrier State," 459.
[145] National Institutes of Health, *NIH Consensus Statement*, 2.
[146] Ibid., 13.
[147] Ibid., 11; Mennuti, Thompson, and Press, "Screening for Cystic Fibrosis Carrier State," 460.
[148] J. A. Kuller, R. Baughman, and C. Biolsi, "Cystic Fibrosis and the National Institutes of Health Consensus Statement: Are Obstetrician-Gynecologists Ready to Comply?" *Obstetrics and Gynecology* 93 (1999): 581. For example, 35 percent of physicians surveyed could not identify the delta F508 mutation as the most frequent CFTR gene mutation, only 43 percent identified the ethnic group with the highest detection rate (Ashkenazi Jewish), and only 16 percent correctly identified the carrier frequency in the African American population. Ibid., 583.
[149] National Institutes of Health, *NIH Consensus Statement*, 15.
[150] Ibid. ("Although assumptions about these variables differed, studies showed that the costs per identified CF fetus averted ranged from $250,000 to $1,250,000 for a Caucasian population of North European ancestry.")

commentator referred to this discussion as an indirect and ethically troubling claim that "screening of this kind represents good value."[151]

### *Adolescent and School-Based Carrier Screening*

Although many agree that the ideal age for identifying carriers for autosomal recessive diseases is in early adulthood, prior to pregnancy initiation, the cystic fibrosis screening studies showed that most individuals are not interested in testing in the absence of personal, concrete, marital, and/or reproductive plans.[152] Some have proposed targeting young adults and adolescents of high-risk populations by school-based screening programs. A few such programs exist.

#### *Dor Yeshorim Screening Program*

In the early 1980s, a premarital Tay-Sachs carrier screening program was adapted for the ultra-Orthodox Jewish community, which is opposed to abortion and contraception.[153] The program, called Chevra Dor Yeshorim, was initiated in New York State; it has since expanded internationally and has tested over 150,000 individuals.[154] Marriages within the ultra-Orthodox Jewish community are generally prearranged, and the program is designed to prevent marriages between two carriers. The program targets twelfth graders in Orthodox Jewish schools to optimize identification of carriers when they are close to marriage age.[155]

Testing is voluntary and confidential and requires parental consent for individuals under age eighteen.[156] Samples are coded and the individuals tested are given their code number only, not a test result. When a potential marriage match occurs, the family of one or both of the partners contacts the program registry and provides both partners' codes.[157] While the program aims to prevent the marriage of two carriers and the birth of infants affected by Tay-Sachs disease, the families and individuals receiving the testing results are free to use the information as they wish. Some credit the program's focus on students for whom marriage is not imminent, and its routine acceptance by the community, with reducing

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[151] Schmidtke, "A Commentary on the NIH Consensus Statement," 54.

[152] American College of Medical Genetics/American Society of Human Genetics, "ASHG/ACMG Report — Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents," *American Journal of Human Genetics* 57 (1995): 1233. The report states that "reproductive benefits may be of limited value . . . to adolescents who are not likely to make family planning decisions primarily on the basis of their genetic status."

[153] For a discussion, see M. Levin, "Screening Jews and Genes: A Consideration of the Ethics of Genetic Screening within the Jewish Community: Challenges and Responses," *Genetic Testing* 3 (1999): 207, 209–210.

[154] Telephone interview with Frances Berkwits, M.S., genetic counselor to the Dor Yehorim program, September 22, 1999. See also B. Merz, "Matchmaking Scheme Solves Tay-Sachs Problem," *Journal of the American Medical Association* 258 (1987): 2636, 2367; Markel, "Scientific Advances and Social Risks," 166–167; Levin, "Screening Jews and Genes," 210; Wingerson, *Unnatural Selection*, 1–20. The phrase Dor Yeshorim, from the Talmud, means "Generation of the Upright." Wingerson, *Unnatural Selection*, 8.

[155] Telephone interview with Frances Berkwits; telephone interview with Rabbi Josef Ekstein, Founder and President, Dor Yeshorim, September 21, 1999. Most young women in the community marry by age nineteen.

[156] Levin, "Screening Jews and Genes," 210.

[157] In some cases, a matchmaker is involved in setting up matches and in contacting the Dor Yeshorim registry, but this has become less common. Telephone interview with Francis Berkwits.

testing-associated anxiety.[158] By identifying only carrier couples, versus all carrier individuals, the program spares the majority of carrier individuals the potential psychosocial risks, including stigmatization, of being identified as a Tay-Sachs carrier.[159]

Some commentators acknowledge the success of the program but contend that it relies upon distinctive features of the Orthodox Hassidic community it serves, including the cohesiveness and apparent mutual consent of a small community, the acceptance of rabbinical endorsements, and the custom of pre-arranged marriage.[160] In 1993 and 1995, the program began testing for three additional disorders.[161]

*Other School-Based Genetic Carrier Screening Programs*

There are other examples of broader school-based carrier screening programs designed to identify carriers as they approach young adulthood and performed outside the United States.[162] For example, for over twenty years, programs in Montreal have targeted high school seniors in population groups at increased carrier risk for Tay-Sachs disease (based on Ashkenazi Jewish background) or beta-thalassemia, a blood disorder common in those of Mediterranean background.[163] Students attend educational sessions and are informed of the rationale for screening; both the student and a parent must consent to testing. Screening reports are presented confidentially to the student by telephone, with offers of additional education and counseling. Since the program was initiated in 1972, the regional incidence of Tay-Sachs disease and beta-thalassemia fell 90 to 95 percent.[164]

The program elicited some criticism in the 1970s, citing concerns about psychological harms to tested students.[165] Responses to a 1996 review of the program, however, were generally favorable. One commentator cited the program's success "without apparent psychological or sociological harm."[166] Another commentator agreed but pointed out that the program may benefit from aspects of the Canadian health care system, such as

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[158] Ibid., Levin, "Screening Jews and Genes," 210.

[159] For identified carrier couples, both partners are identified as carriers. The majority of screened carriers, however, will not be informed of their (and their family's) carrier status because their partner will test negative, eliminating the need to notify them. If tested on an individual basis, they would be notified.

[160] Wingerson, *Unnatural Selection*, 11–12; Hepburn, "Genetic Testing and Early Diagnosis," 108.

[161] Levin, "Screening Jews and Genes," 210; see also page 130, this chapter.

[162] See A. G. Motulsky, "Screening for Genetic Diseases," *New England Journal of Medicine* 336 (1997): 1314; L. McCabe, "Invited Editorial: Efficacy of a Targeted Genetic Screening Program for Adolescents," *American Journal of Human Genetics* 59 (1996): 762; Rowley, Loader, and Levenkron, "Cystic Fibrosis Carrier Population Screening," 56.

[163] J. J. Mitchell et al., "Twenty-Year Outcome Analysis of Genetic Screening Programs for Tay-Sachs and Beta-Thalassemia Disease Carriers in High Schools," *American Journal of Human Genetics* 59 (1996): 793.

[164] Ibid., 793.

[165] See P. J. Edelson, "The Tay-Sachs Disease Screening Program in the U.S. as a Model for the Control of Genetic Disease: An Historical View," *Health Matrix: Journal of Law-Medicine* 7 (1997): 125.

[166] Motulsky, "Screening for Genetic Diseases," 1315.

the ability of individuals age fourteen or older to seek health care on their own and reduced concerns about loss of insurance coverage because of universal health care coverage.[167]

Another high school-based carrier screening program, this one for alpha and beta thalassemia, was implemented in Hong Kong.[168] The program targeted students fourteen to nineteen years of age and required parental consent, which was received for about 75 percent of eligible students. The program reportedly involved less community consultation and education than the Montreal program.

## Screening for Susceptibility to Late-Onset Disorders

Generally, genetic testing to determine risks for late-onset disorders is offered only to individuals identified to be at greater risk than the general population for a particular disease based on their family and/or personal history. Commentators predict that in the future, however, DNA-based testing technologies may lead to population-based genetic screening to assess risk for some adult-onset disorders.[169] Population-based screening programs could be offered to the general population or to select populations perceived to be at higher risk for specific disorders (for example, based on racial or ethnic background or on workplace environmental exposures).[170]

One example of population-based marketing of a genetic test occurred in 1996, when a commercial laboratory promoted BRCA1 gene testing for a mutation estimated to have a 1 percent prevalence among women of Ashkenazi Jewish descent.[171] The laboratory targeted the offering of the test to all Ashkenazi Jewish women, regardless of their family and/or personal history.[172] Many in the genetics community considered this approach premature, citing the test's uncertain predictive powers and the lack of established clinical interventions.[173]

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[167] McCabe, "Efficacy of a Targeted Genetic Screening Program," 762.

[168] Y. L. Lau et al, "Prevalance and Genotypes of Alpha and Beta Thalassemia Carriers in Hong Kong — Implications for Population Screening," *New England Journal of Medicine* 336 (1996): 1298; see also Motulsky, "Screening for Genetic Diseases," 1315–1316.

[169] See, e.g., Beaudet, "Making Genomic Medicine a Reality," 1; Collins, "Medical and Societal Consequences of the Human Genome Project," 28.

[170] For a discussion of screening, see Chapter 2, page 30.

[171] "The Risk of Cancer Associated with Specific Mutations of BRCA1 and BRCA2 among Ashkenazi Jews," *New England Journal of Medicine* 336 (1997): 1401; F. H. Fodor et al., "Frequency and Carrier Risk Associated with Common BRCA1 and BRCA2 Mutations in Ashkenazi Jewish Cancer Patients," *American Journal of Human Genetics* 63 (1998): 45.

[172] G. Kolata, "Breaking Ranks, Lab Offers Test to Assess Risk of Breast Cancer," *New York Times*, April 1, 1996, A1; S. Lehrman, ". . . As Concern Grows over Screening," *Nature* 384 (1996): 297.

[173] Lehrman, ". . . As Concern Grows over Screening"; American College of Medical Genetics, "Statement on Population Screening for BRCA-1 Mutation in Ashkenazi Jewish Women," 1996, American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/pol-24.htm*, visited December 16, 1998. The statement cites the need for more data about the predictive value of the test. For further discussion of the test's predictive value for different persons and populations, see page 126, this chapter; see also Chapter 3, page 65.

## Possible Candidate Screening Tests

A strong candidate condition for population-based genetic screening is hemochromatosis, an adult-onset disorder caused by excessive iron uptake, leading to iron "overload" and possibly to liver cirrhosis, diabetes, heart disease, and other clinical complications.[174] It is an autosomal recessive disorder, affecting individuals who inherit two mutant copies of a gene called HFE, discovered in 1996.[175] Among Caucasian and Hispanic populations, the estimated prevalence of iron overload due to hemochromatosis is about 1 per 200;[176] among African Americans it is less than 1 per 1,000.[177] It is one of the few identified adult-onset genetic disorders for which simple effective therapy exists: removal of blood iron by phlebotomy (regular bloodletting).[178]

Prior to the discovery of the HFE gene, several groups had recommended population screening of serum iron measures to identify those at risk for hemochromatosis.[179] Following discovery of the HFE gene and identification of particular gene variants linked to hemochromatosis, some proposed DNA-based population screening. In response, the Centers for Disease Control and Prevention (CDC) and the National Human Genome Research Institute (NHGRI) sponsored a meeting to evaluate the role of genetic screening for hemochromatosis.[180] The panel concluded unanimously that it would be premature to implement population-based DNA screening because of (1) limitations of the test's predictive power, based on evidence that other hemochromatosis-associated genes may exist and evidence that some individuals who inherit two mutant copies of the HFE gene remain asymptomatic,[181] and (2) concerns regarding possible stigmatization and discrimination against those who test positive. Following this report, the National Heart, Lung, and Blood Institute implemented a five-year, multiethnic, multicenter study to address the scientific and clinical uncertainties of hemochromatosis screening and to identify the feasibility, benefits, and risks of screening.[182]

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[174] W. Burke et al., "Hereditary Hemochromatosis: Gene Discovery and Its Implications for Population-Based Screening," *Journal of the American Medical Association* 280 (1998): 172.

[175] J. N. Feder et al., "A Novel MHC Class-I-Like Gene Is Mutated on Patients with Hereditary Hemochromatosis," *Nature Genetics* 13 (1996): 399.

[176] M. Shannon et al., "Screening for Hemochromatosis in Primary Care Settings," *Annals of Internal Medicine* 129 suppl. (1998): 962.

[177] M. E. Cogswell et al., "Iron Overload, Public Health, and Genetics: Evaluating the Evidence for Hemochromatosis Screening," *Annals of Internal Medicine* 129 suppl. (1998): 971.

[178] Burke et al., "Hereditary Hemochromatosis," 173.

[179] See ibid. Persistent increase in serum iron measures, in the absence of other causes, provides a "presumptive diagnosis" for the disorder.

[180] Ibid., 172, 175–177.

[181] Ibid.; see also Cogswell et al., "Evaluating the Evidence for Hemochromatosis Screening"; A. S. Tavill et al., "Clinical Implications of the Hemochromatosis Gene," *New England Journal of Medicine* 341 (1999): 755. These limitations are the two general limitations of DNA-based tests, genetic heterogeneity and incomplete penetrance. See Chapter 2, page 41.

[182] National Heart, Lung, and Blood Institute website: *http://nhbli.nih.gov/nhbli/rafs/rfp9903.htm*, visited February 1, 1999.

Some commentators also have recommended population-based screening for alpha-1 antitrypsin disorder, an autosomal recessive genetic condition that greatly increases susceptibility to cigarette smoking-related chronic lung disease.[183] The argument for screening is that "knowledge is power" and that provision of definitive risk information to susceptible individuals may promote risk avoidance and reduce disease.[184] One commentator supported this view by citing a study performed in Denmark, in which 67 percent of individuals informed that they were susceptible to this genetic disorder reportedly quit smoking.[185]

Genetic tests that detect lower risk susceptibility gene mutations for which preventive interventions are available also may eventually be offered on a population basis, although some question the value of screening when the degree of risk is low.[186] One example is a particular gene variant in the APC gene, known as the I130K variant, that is estimated to occur in about 6 percent of the Ashkenazi Jewish population and to increase risk for colon cancer approximately two-fold, from a general population lifetime risk of 5 percent, or one in twenty.[187] Despite the marginal increase in disease risk, this test could be offered as a population screening test, provided it shows appropriate clinical validity and utility.[188]

### Special Issues for Genetic Screening for Late-Onset Disorders

Models for predictive genetic screening exist for reproductive and newborn screening; in both cases, screening is performed to determine risk for single-gene disorders for which inheritance of one or a pair of mutant gene variants results in a 100 percent chance of disease.[189] In contrast, no established models for predictive genetic screening of adults, or for susceptibility gene variants, yet exist. In the future, however, screening tests for hemochromatosis and for susceptibility variants that may increase risk for more common late-onset disorders may enter mainstream clinical care. Before such screening tests are offered, however, the principles derived over several decades for both newborn and reproductive genetic testing must be similarly considered. Screening tests must have a clearly defined purpose and high analytical validity,[190] and they must be offered with appropriate education, counseling, informed consent, and confidentiality protections. In addition, levels of a test's clinical validity and utility may need to be higher when these tests are offered to predict disease risks to healthy populations.

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[183] Beaudet, "Making Genomic Medicine a Reality," 5; for discussion of alpha-1 antitrypsin disorder, see Chapter 3, page 66.
[184] See J. T. Wilcke, "Late Onset Genetic Disease," 744.
[185] Ibid.
[186] See Beaudet, "Making Genomic Medicine a Reality," 9.
[187] S. J. Laken et al., "Familial Colorectal Cancer in Ashkenazim Due to a Hypermutable Tract in APC," *Nature Genetics* 17 (1997): 79; see also G. F. Petersen et al., "Genetic Testing and Counseling for Hereditary Forms of Colorectal Cancer," *Cancer* 86 suppl. (S8) (1999): 1720, 1722, 1728. APC stands for adenomatous polyposis coli.
[188] See, e.g., F. Gilbert, "Establishing Criteria for a Carrier Detection Panel: Lessons from the Ashkenazi Jewish Model," *Genetic Testing* 2 (1998): 301, 303.
[189] For a discussion of single-gene disorders, see Chapter 1, page 14.
[190] See page 104, this chapter.

### *Predictive Value of the Screening Test*

A test's predictive value — the chance that someone testing positive will get a disease and that someone testing negative will not — may differ when the tested individual is someone with known familial risk versus someone in the general population. The possibility of clinical false positive results is especially high for genetic tests that detect susceptibility mutations to determine risks for disorders that are not fully penetrant, such as BRCA susceptibility mutations. BRCA gene testing was developed from research involving families in which four or more members had breast and/or ovarian cancer. Subsequent research showed that while BRCA gene testing of a woman with a strong family history of breast and/or ovarian cancer who learns she has inherited the familial mutation confirms her high risk, individuals without a strong family history who test positive may be at significantly lower risk.[191] An inability to adequately interpret BRCA gene test results outside of high-risk families contributed to one biomedical policy group's conclusion that "general population screening clearly cannot be justified."[192] The possibility of false negative test results also is greater when a family mutation has not been identified.[193]

Similar to DNA-based carrier testing for cystic fibrosis, the clinical predictive value of some late-onset predictive tests also may vary for different populations when a limited number of all possible mutations are targeted by the test.[194] For example, APOE gene testing data that indicate increased risk for late-onset Alzheimer disease associated with inheritance of a particular gene variant were gathered from individuals of Northern European descent and may not be valid for persons of other geographic or racial derivation.[195] Before a predictive genetic test is applied to the general population, it is critical that sufficient research be performed to establish the test's predictive value for members of that population.

### *Clinical Utility*

Another important consideration is whether the offering of a predictive genetic screening test should require availability of a medical preventive or treatment intervention. In the absence of such a benefit, members of the general population who perceive themselves to be at low disease risk and test positive for a susceptibility mutation might experience more psychological distress than someone from a high-risk

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[191] See Chapter 3, page 64.
[192] B. A. Koenig et al., "Genetic Testing for BRCA1 and BRCA2: Recommendations of the Stanford Program in Genomics, Ethics, and Society," *Journal of Women's Health* 7 (1998): 531, 537.
[193] See Chapter 3, page 64.
[194] See page 119, this chapter.
[195] See Chapter 3, page 67.

family.[196] While some predict that genetic screening tests might be offered in the absence of available interventions,[197] others think that tests should be restricted to those that predict risk for treatable or preventable disorders.[198] In addition to providing a direct medical benefit, the existence of a confirmed intervention also would be likely to reduce concerns that persons identified to have susceptibility mutations would be subject to psychosocial or discrimination risks.[199]

### *Interpretation of Test Results*

A key concern for the introduction of predictive genetic tests generally is the common misperceptions about the meaning of test results.[200] This concern is of special relevance for screening apparently healthy persons to detect susceptibility gene variants for common late-onset disorders. While inheritance of such a gene variant may significantly increase an individual's risk for disease relative to the general population (relative risk), the actual lifetime risk that any such individual will develop the associated disease may be quite low. For example, persons of Ashkenazi Jewish descent who test positive for the I130K variant of the APC gene have an increase in their relative colon cancer risk of two-fold, or 100 percent.[201] Overall lifetime risk, however, is only about 10 percent, versus a general population lifetime risk of 5 percent.[202] Providers must be able to adequately convey risk data such that those testing positive do not misunderstand or overinterpret results that convey increased risk. It is equally important that individuals who learn that they are not at increased relative risk based on genetic testing (e.g., for breast cancer) understand that they are not free of future disease risk and that baseline medical surveillance measures (e.g., routine mammography) and healthy behaviors are still prudent.

## Multiplex Testing

Multiplex genetic testing is predictive testing for two or more completely different conditions in a single testing session.[203] The multiple tests offered together may be performed as separate laboratory tests or may be performed together in a single laboratory testing session.[204] One longstanding form of multiplex genetic testing is newborn screening that tests newborns for a panel of serious congenital disorders for which immediate preventive interventions are available and require immediate implementation.[205] More recently, multiplex tests have been created to screen for

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[196] See page 104, this chapter.
[197] See, e.g., Collins, "Medical and Societal Consequences of the Human Genome Project."
[198] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 47; see also Beaudet, "Making Genomic Medicine a Reality," 6.
[199] Beaudet, "Making Genomic Medicine a Reality," 6.
[200] See Chapter 4, page 91.
[201] Petersen et al., "Genetic Testing and Counseling for Hereditary Forms of Colorectal Cancer," 1722.
[202] Ibid., 1728. The article states that general population risk for colon cancer is 5 percent.
[203] American Medical Association Council, "Multiplex Genetic Testing," 15.
[204] The latter form of testing may become more common with the development of DNA chip and related technologies that can scan for thousands of mutations in a single assay. See Chapter 2, page 45.
[205] For a discussion of newborn screening, see Chapter 6. Newborn screening panels also test for some nongenetic congenital disorders.

reproductive carrier status for autosomal recessive disorders,[206] and some commentators predict that commercial forces and DNA chip technologies[207] will drive the creation of multiplex panels for late-onset predictive testing.[208]

Multiplex testing in effect moves a genetic test from the individual "at-risk" model to a population-based screening model — tests are grouped together to be offered to whole populations, not to particular individuals based on their family and/or personal medical histories. This may be beneficial, provided the tests meet established criteria and efficacious preventive options exist.[209] Some commentators, however, have expressed concerns about criteria for grouping tests together, implications for the counseling and informed consent process, and the potential for discrimination based on test results.[210]

### Multiplex Prenatal Carrier Test Panels

Many medical centers and genetic testing laboratories now offer multiplex panels for prenatal carrier testing for autosomal recessive disorders that have a high incidence in the Ashkenazi Jewish population and for which reliable testing is available. The targeting of this particular population is because of the identification of a limited number of Ashkenazi Jewish "founder mutations" that account for the vast majority of certain single-gene disorders that occur with high frequency in that population. For example, in this population, a total of ten mutations in three genes accounts for 97 percent of cystic fibrosis and Tay-Sachs disease and 98 percent of Canavan disease,[211] another incurable, progressively neurodegenerative disorder that is often fatal in childhood.[212]

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[206] See page 105, this chapter.

[207] See Chapter 2, page 45.

[208] American Medical Association Council, "Multiplex Genetic Testing," 19–21; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 27, 297; S. Elias and G. J. Annas, "Generic Consent for Genetic Screening," *New England Journal of Medicine* 330 (1994): 1611; Collins, "Medical and Societal Consequences of the Human Genome Project."

[209] See page 106, this chapter.

[210] American Medical Association Council, "Multiplex Genetic Testing," 15; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 27, 102, 298. For discussion of informed consent for multiplex testing, see Chapter 7, page 192.

[211] See *Molecular Genetics Testing at New York University Medical Center: Ashkenazi Jewish Genetic Disease Screen*, New York University Medical Center website: *http://humgen-www.med.nyu.edu/Hgenetics/AJGDS.html*, visited December 31, 1998.

[212] R. Matalon and K. Michals-Matalon, "Prenatal Diagnosis of Canavan Disease," *Prenatal Diagnosis* 19 (1999): 669. Both the American College of Medical Genetics and the American College of Obstetricians and Gynecologists recommend that carrier screening for Canavan disease, as well as Tay-Sachs disease, be offered to Ashkenazi Jewish women and couples who are pregnant or, ideally, to those considering pregnancy. American College of Medical Genetics, "Position Statement on Carrier Testing for Canavan Disease," June 1998, American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/pol-31.htm*, visited March 3, 2000; American College of Obstetricians and Gynecologists Committee on Genetics, "ACOG Committee Opinion: Screening for Canavan Disease," *International Journal of*

Several academic and commercial genetic testing laboratories, and the Dor Yeshorim program,[213] offer multiplex carrier screening panels for three or more disorders.[214] For example, in 1995, one academic genetic testing laboratory in New York City began offering a "Jewish Genetic Disease Carrier Program," originally offering testing for Tay-Sachs disease and cystic fibrosis.[215] The screening panel has since expanded to include testing for Canavan disease, Niemann-Pick disease, and Gaucher disease; patients can choose which tests they wish to have performed. Within the program, almost 100 percent of patients offered the screening panel accept it.[216]

The appearance and expansion of such carrier testing panels have raised questions about what types of screening tests should be routinely offered and how tests should be bundled within a single panel. Some disorders, for example, Tay-Sachs disease, Canavan disease, and Niemann-Pick disease,[217] all neurodegenerative disorders that generally are lethal in childhood, are generally accepted as appropriate to offer together.[218] Inclusion of other tests into such a panel, however, may provoke controversy because of variable disease severity, range of symptoms, and existence of possible treatment options. For example, cystic fibrosis is classified by some as a lethal disorder and by others as a nonlethal disease of variable and significant morbidity.[219] Another is deafness due to inheritance of two mutated copies of a gene called connexin 26.[220] Deafness, unlike Tay-Sachs disease and Canavan disease, is a limited disability, not a fatal and incurable neurodegenerative disorder.[221]

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*Obstetrics and Gynecology* 65 (1999): 91. The estimated carrier frequency in the Ashkenazi Jewish population is one in forty.

[213] Telephone interview with Rabbi Josef Ekstein, September 21, 1999; the Dor Yeshorim program has expanded to test for carrier status for additional autosomal recessive disorders, including cystic fibrosis, Canavan disease, and Fanconi anemia type C. See also J. M. DeMarchi, C. T. Caskey, and C. S. Richards, "Population-Specific Screening by Mutation Analysis for Diseases Frequent in Ashkenazi Jews," *Human Mutation* 8 (1996): 116.

[214] See, e.g., C. M. Eng et al., "Prenatal Genetic Carrier Testing Using Triple Disease Screening," *Journal of the American Medical Association* 278 (1997): 1268; D. Kronn, V. Jansen, and H. Ostrer, "Carrier Screening for Cystic Fibrosis, Gaucher Disease, and Tay-Sachs Disease in the Ashkenazi Jewish Population," *Archives of Internal Medicine* 158 (1998): 777; Gilbert, "Establishing Criteria for a Carrier Detection Panel," 301.

[215] Gilbert, "Establishing Criteria for a Carrier Detection Panel," 301.

[216] Ibid.

[217] E. H. Schuman and S. R. P. Miranda, "Niemann-Pick Disease: Mutation Update, Genotype/Phenotype Correlations, and Prospects for Genetic Testing," *Genetic Testing* 1 (1997): 13.

[218] Gilbert, "Establishing Criteria for a Carrier Detection Panel," 301. See also American College of Medical Genetics, "Position Statement on Carrier Testing for Canavan Disease"; American College of Obstetricians and Gynecologists Committee on Genetics, "ACOG Committee Opinion: Screening for Canavan Disease."

[219] Gilbert, "Establishing Criteria for a Carrier Detection Panel," 302; see also page 118, this chapter.

[220] R. J. Morrell et al., "Mutations in the Connexin 26 Gene among Ashkenazi Jews with Syndromic Deafness," *New England Journal of Medicine* 339 (1998): 1500.

[221] See Gilbert, "Establishing Criteria for a Carrier Detection Panel," 303.

Another and controversial example is Gaucher disease. This autosomal recessive disorder has a carrier rate of about one in fourteen in the Ashkenazi Jewish community,[222] and five mutations account for 95 percent of cases.[223] The majority of individuals who inherit two gene copies bearing these mutations, however, are only minimally affected,[224] with one study suggesting that the majority of affected persons never come to medical attention.[225] In fact, Ashkenazi Jewish carrier multiplex testing has identified asymptomatic prospective parents who themselves carry two mutant copies of the Gaucher disease associated gene.[226] Mutation analysis for Gaucher disease offers limited prognostic information because even individuals with the same gene mutations can have very different clinical courses.[227]

There also is an encouraging form of enzyme replacement therapy for Gaucher disease, although it is very expensive.[228] The possibility of treatment, along with the disease's variable severity, led at least one screening program, Dor Yeshorim, to decide against including Gaucher disease in its testing panel.[229] In 1995, the same considerations led an NIH Technology Assessment Panel to recommend against widespread population-based carrier screening for Gaucher disease, although they did state that peer-reviewed pilot studies may be appropriate for some communities.[230]

## Multiplex Testing for Late-Onset Disorders

Dr. Francis Collins, Director of the National Human Genome Research Institute, projects that, by the year 2010, healthy young adults might routinely be offered multiplex testing panels to determine future disease risks.[231] He speculates that testing might be offered when it is likely to reveal a two-fold or higher difference in individualized risk from that of the general population. He also speculates that there may be separate panels to test for disease risks for which established clinical interventions are available and those for which interventions are not available.

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[222] J. Charrow et al., "Gaucher Disease: Recommendations on Diagnosis, Evaluation, and Monitoring," *Archives of Internal Medicine* 158 (1998): 1754, 1755.

[223] National Institutes of Health Technology Assessment Conference Statement, "Gaucher Disease: Current Issues in Diagnosis and Treatment," *Journal of the American Medical Association* 158 (1998): 548, 550.

[224] Gilbert, "Establishing Criteria for a Carrier Detection Panel," 302–303.

[225] See ibid., 302–303; J. Azuri et al., "Asymptomatic Gaucher Disease: Implications for Large Scale Screening," *Genetic Testing* 2 (1998): 297.

[226] DeMarchi, Caskey, and Richards, "Population-Specific Screening by Mutation Analysis for Diseases Frequent in Ashkenazi Jews," 122; Kronn, Jansen, and Ostrer, "Carrier Screening for Cystic Fibrosis, Gaucher Disease, and Tay-Sachs Disease," 779.

[227] National Institutes of Health Technology Assessment Conference Statement, "Gaucher Disease: Current Issues in Diagnosis and Treatment," 549, 551.

[228] Ibid. Enzyme replacement therapy costs range from $100,000 to $400,000 per patient annually.

[229] Testing may be performed, however, based on specific request by a family.

[230] National Institutes of Health Technology Assessment Conference Statement, "Gaucher Disease: Current Issues in Diagnosis and Treatment," 551.

[231] Collins, "Medical and Societal Consequences of the Human Genome Project," 34–35.

Multiplex panels for susceptibility tests to determine relative risk for late-onset disorders also might be grouped by other factors, including age of disease onset,[232] degree of disease risk (low risk versus high risk), disease classifications (e.g., cancers, neurodegenerative disorders, mental disorders), and race or ethnicity (e.g., for identified susceptibility mutations that occur in individuals of Ashkenazi Jewish background). Some have suggested that from a list of available tests, individuals could choose to be tested and obtain risk information for a selected subset of tests.[233]

In addition to panels for predicting disease risks, one commentator projects the construction of "pharmacogenetic" testing panels to individualize risk-benefit assessments for prescribing medications.[234] Genetic testing panels also could be used to guide specific medical decisions; for example, a woman making decisions about estrogen replacement therapy might wish to ascertain her genetic (in addition to nongenetic) risk for disorders that may be affected by estrogen therapy, including breast cancer, cardiovascular disease, osteoporosis, and Alzheimer disease.

### Policy Issues

The American Medical Association Council on Ethical and Judicial Affairs (AMA Council) stated that physicians should not order tests for multiple genetic conditions unless the tests are clinically relevant to the particular patient.[235] The IOM Committee opposed "the multiplexing of all available genetic tests merely because it is technologically possible to do so."[236] It acknowledged, however, that multiplex panels will be developed in the future and stated that innovative methods are needed to group tests by relative types of disorders that raise similar issues.[237] The AMA Council also noted that in general medical practice, it is often less expensive and equally convenient to order batteries of tests rather than individual tests and that there may be incentives to promote bundled genetic testing.[238]

A key issue for both reproductive and late-onset multiplex testing will be how to bundle tests together to allow for adequate pretest education, counseling, and consent.[239] An initial approach to bundling, based on the relative ease of identifying founder mutations among racial and ethnic groups, resulted in the creation of the Ashkenazi Jewish carrier panels. This approach is understandable at the present state of knowledge about human gene variants, when such founder mutations common to defined

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[232] Beaudet, "Making Genomic Medicine a Reality," 6.
[233] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 259; Gilbert, "Establishing Criteria for a Carrier Detection Panel," 303.
[234] Beaudet, "Making Genomic Medicine a Reality," 4; for a discussion of phamacogenetic testing, see Chapter 3, page 74.
[235] American Medical Association Council, "Multiplex Genetic Testing," 21.
[236] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 298.
[237] Ibid., 27.
[238] American Medical Association Council, "Multiplex Genetic Testing," 18.
[239] For further discussion, see Chapter 7, page 192.

geographic/social populations are more readily identifiable than other human gene mutations.[240]

However, this approach to forming multiplex panels can complicate an already complex set of issues. The population genetics that enable construction of panels for the Ashkenazi Jewish population relies on a history of reproductive isolation that will not apply for many groups and that may become even more complex with successive generations.[241] Also, the AMA Council stated that such targeted testing relies upon a patient's self-identification with cultural features that do not always correspond to genetic inheritance and, that while ethnic considerations may be appropriate in some circumstances, such considerations generally categorize patients rather than meet distinct needs and, in so doing, risk being discriminatory.[242]

For late-onset genetic testing, the IOM Committee stated that tests for untreatable disorders should not be multiplexed with tests for disorders that can be cured or prevented by treatment or avoidance of particular environmental stimuli.[243] Another commentator stated that for creation of multiplex panels to predict risk for late-onset disorders, "the single most important variable . . . is the need for effective interventions for those individuals identified as having specific genotypes."[244] He noted, however, that grouping tests into two distinct categories, based on whether a useful intervention exists, may not be simple. For example, some tests may disclose disease risks for which only partially effective interventions exist and for which it may be more difficult to balance the risks and benefits of screening.[245]

Related concerns arise when considering creation of multiplex testing panels for reproductive purposes. While many commentators agree that it is appropriate to offer screening for disorders such as Tay-Sachs disease, which uniformly results in early childhood death, many disagree about the implications of tests for disorders that are more variable in their severity, occurrence, or treatability. One commentator, for example, suggests that one way for grouping tests may be by disease characteristics, including disease mortality, morbidity, and whether a disorder causes neurodegeneration (and associated mental retardation).[246]

Others suggest that different panels might test for physical abnormalities, mental abnormalities, or both.[247] Some predict that prenatal carrier testing panels may expand even beyond testing for risks of infancy or childhood-onset single-gene disorders, to include tests

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[240] See, e.g., Beaudet, "Making Genomic Medicine a Reality," 4.
[241] See American Medical Association Council, "Multiplex Genetic Testing," 19.
[242] Ibid., 19–20.
[243] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 276.
[244] Beaudet, "Making Genomic Medicine a Reality," 6.
[245] Ibid.
[246] Gilbert, "Establishing Criteria for a Carrier Detection Panel," 304.
[247] Annas and Elias, "Generic Consent for Genetic Screening," 1612.

for late-onset susceptibility disorders, for example, BRCA testing for adult-onset breast cancer.[248] Some have argued that such testing is inappropriate and should not be offered as part of a multiplex screening panel.[249] One experienced provider stated, however, that for disorders that strike during infancy or childhood, parents want the opportunity to "decide whether or not to be carrier tested and for what."[250]

## Conclusions and Recommendations

### Purpose of Predictive Genetic Screening

**The purpose of predictive genetic screening should be to benefit the individual or couple tested. Screening tests offered to healthy individuals who do not perceive themselves or their offspring to be at increased risk for disease based on family and/or personal history should provide clear medical benefits or expanded reproductive options.**

We agree with others that the primary benefit of genetic screening tests should be to the individuals or couples tested and that testing should provide individuals with expanded medical or reproductive options. Societal cost savings are not a sufficient reason to offer them.

### Predictive Value of Screening Tests

**Predictive genetic screening tests should have a sufficient level of confirmed predictive value in healthy populations to justify their use for individuals who are not known to be at increased disease risk.**

When a genetic test is offered as a screening test for healthy populations, as opposed to a clinically indicated test for individuals identified to be at high risk based on family and/or personal history, levels of both positive and negative predictive value of the test may differ. The use of a test for a general population, versus for a group that is at relatively higher risk than the general population for a true positive result, generally results in higher numbers of false positive results. There are additional concerns for the predictive value of genetic tests to determine risks for disorders that are not fully penetrant, such as BRCA testing. In such cases, the effect of other genetic and environmental factors, often unknown, will generally lower the test's positive predictive value when used to screen persons who do not have a strong family history of the disease. Also, the performance of DNA-based screening tests to detect only some of all possible mutations of a particular gene may lead to significant numbers of false negatives and different rates of false negatives for persons from different ethnic or racial backgrounds. Before a predictive genetic test is offered as a screening test, it is critical that sufficient research be performed to confirm that a test has

[248] Ibid., 1613.
[249] Gilbert, "Establishing Criteria for a Carrier Detection Panel," 304; Annas and Elias, "Generic Consent for Genetic Screening," 1613.
[250] Gilbert, "Establishing Criteria for a Carrier Detection Panel," 303.

sufficiently high predictive value for the members of the population to whom the test is offered.

## How to Offer Predictive Genetic Screening Tests

**Predictive genetic screening tests should be voluntary and should be offered only when accompanied by adequate education, counseling, informed consent, test follow-up, and efforts to ensure confidentiality.**

When a screening test has sufficient analytical and clinical validity, when testing provides persons with useful medical or reproductive options, and when the risk of inappropriate uses of test results is minimal, it is likely that most individuals would benefit from predictive genetic screening. However, as more tests and improved testing technologies become available, the types of tests offered and the benefits they may provide will occur along a continuum with respect to seriousness of diseases screened for, relative degree of risk, and the nature and degree of the benefits associated with preventive interventions.

Based on these factors, reasonable persons might differ as to whether they wish to undergo a particular screening test. It is critical that individuals who are offered screening tests receive full pretest education and counseling, as well as appropriate posttest counseling and follow-up. To assure this, adequate professional education of health care providers must precede the offering of genetic screening tests.[251] It is essential that providers obtain informed consent. The need for informed consent is heightened by the fact that routinely offered screening, even though it is not mandatory, may pressure individuals to undergo testing that they might not have elected in another context. Because of the potential for testing-associated discrimination, those offering screening tests should ensure confidentiality of testing and test results.

## Special Concerns about Offering Genetic Screening to Determine Risks for Late-Onset Disorders

**Genetic screening tests to determine future risk for late-onset disorders should have confirmed clinical utility, and screening should be offered on an age-appropriate basis to ensure maximum medical benefit and minimal risks.**

The benefits of offering predictive genetic screening should outweigh the risks, which include the potential harms of psychosocial distress, discrimination, and harms based on adoption of insufficiently tested, and possibly irreversible, medical interventions. The chief benefit of predictive genetic screening is the ability to prevent or mitigate the onset of the disease by initiating medical interventions before symptoms arise. For individuals who are at high risk of developing particular diseases based on their family and/or personal

[251] For further discussion, see Chapter 12.

history, another important potential benefit of predictive testing is the reduction of uncertainty and facilitation of future planning based on test results. The reduction of uncertainty, however, is not an issue for healthy persons with no family history of a particular disease. In the absence of available medical interventions, therefore, there is no reason to offer predictive genetic tests as part of a general screening program.

Timely offering of screening tests also is important to minimize testing-associated risks. In general, screening tests should not be offered until the test result information will be useful to the person tested, generally at the time when a preventive intervention must be implemented to provide a medical benefit.

### Special Concerns about Offering Genetic Screening to Determine Reproductive Risks

**Genetic screening tests to predict reproductive risks should provide individuals and couples with useful options. Providers should make clear that despite the routine offering of tests, some individuals may wish to decline if they think that the test will not be useful to them. Providers should offer screening tests in a timely manner to maximize the reproductive options of tested individuals.**

The eugenic programs of the past, as well as the history of mandatory carrier screening programs and laws, show that misguided or poorly conceived programs and tests can cause serious harms to individuals and groups.[252] Based on these concerns, it is essential that reproductive screening tests expand reproductive options and promote the autonomous reproductive choices of individuals and couples tested. Governmental and societal pressures, including economic pressures, should not influence those autonomous decisions.

Prenatal maternal serum screening, while not meeting the strict definition of a genetic test used in this report, is a screening test to identify those at higher risk for fetal disorders. Results from this screening test and follow-up prenatal tests, including fetal chromosomal analysis, can cause significant anxiety and provide uncertain results that some people may prefer not to confront. Accordingly, providers should offer these and other prenatal tests, including prenatal carrier tests, with adequate education and counseling about the possible outcomes and options and should obtain meaningful informed consent.

We agree with the IOM Committee that, ideally, carrier screening should be offered before individuals attempt to conceive. Providers of routine gynecological health care services should discuss with their patients of reproductive age the availability of carrier screening, as well as health behaviors that promote fetal health (e.g., folic acid nutritional supplements), prior to establishment of pregnancy. We acknowledge, however, the findings of research studies that show that most individuals are not interested in carrier testing for cystic fibrosis unless they are pregnant or planning a pregnancy.[253] Thus, we agree with the

[252] See page 114, this chapter; see also Chapter 4, page 80.
[253] See page 119, this chapter.

NIH Consensus Panel that carrier screening should be offered to pregnant women and their partners.

### Federal and State Governments Should Not Require Genetic Screening by Law

**It is generally inappropriate for federal or state governments to mandate population genetic screening. New York State should repeal legislation that mandates sickle cell carrier screening for some couples seeking a marriage license.**

Government-mandated genetic screening can be justified only in special circumstances, such as screening of newborns to prevent serious and irreparable harm that could not otherwise be avoided.[254] For other forms of genetic screening, especially for screening to determine reproductive risks, it is difficult to envision a sufficient justification for mandated screening.

The history of misguided, although perhaps well-intentioned, sickle cell screening legislation passed in states in the 1970s serves as a reminder of the very real harms of such approaches. The misguided and inappropriate 1972 New York State legislation that required testing of applicants for marriage licenses for the purpose of "discovering the existence of sickle cell anemia" for persons "not of the Caucasian, Indian, or Oriental race,"[255] even though not enforced, should be repealed.

### Role of Study Panels and Professional Guidelines

**Study panels that include national experts, community representatives, and others, as well as professional medical societies such as the American College of Obstetricians and Gynecologists and the American College of Medical Genetics, should determine the appropriateness of offering specific genetic screening tests based on the test's validity and utility. For reproductive screening tests, for which follow-up options may include decisions about pregnancy termination, professional guidelines should consider the seriousness of the disorder tested for, its penetrance, its age of onset, and the variability of disease symptoms.**

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[254] For a discussion of newborn screening, see Chapter 6.
[255] N.Y.S. C.L.S. Dom Rel § 13-aa.

While government agencies may easily ascertain whether a predictive genetic test has sufficient analytical validity, decisions about a test's clinical validity and clinical utility will be more complex and will require specific research. Specially designated professional study panels, as well as professional societies, can provide the necessary analysis at the appropriate time to guide providers about when screening tests should be offered to the general population (or to designated populations) as the standard of care.

For single-gene disorders and especially for more complex disorders, these types of studies will be critical. Once sufficient data are collected, professional society guidelines can educate and advise clinicians, thereby helping to establish standards of care. For example, ACOG guidelines have been instrumental in developing the standard of care for maternal serum screening and for carrier testing for sickle cell disease, Tay-Sachs disease, and Canavan disease.

In the area of reproductive genetics, special considerations may apply. Tests are available for disorders with a range of severity, penetrance (the chance that someone who inherits a gene variant will develop a particular disease), and age of onset. Other tests will likely become available for traits and conditions that do not involve serious morbidity or mortality in early childhood. Available tests vary from tests for uniformly lethal disorders (e.g., Tay-Sachs disease) to disorders with very variable severity (e.g., Gaucher disease) to non-life-threatening disabilities, such as deafness. Tests for late-onset susceptibility gene variants (e.g., BRCA, or future identified susceptibility variants for late-onset mental disorders) might also be considered. Professional guidelines therefore should consider a complex array of factors, including type of disease or impairment, degree of morbidity and mortality, existence of treatments, and age of onset of disease.

### Genetic Screening of Minors

**Generally, minors should not be offered genetic screening tests to determine future health or reproductive risks, unless screening provides a clear and timely medical benefit and has minimal psychosocial risks.**

Genetic screening of children who are at no known family or personal risk should not be offered unless there is a clear medical benefit to the minor. While school-based programs may ensure reproductive carrier testing of most individuals prior to reproduction, we believe that the lack of utility of that information to most minors, and the potential risks associated with testing positive, shifts the balance of potential benefits and risks in a negative direction. We recognize that some exceptions may exist, such as the Dor Yeshorim program, in which contained communities with shared and unique beliefs and customs, including arranged marriage and acceptance of rabbinical authority, make possible a school-based program to screen older adolescents with their parents' consent.

**Multiplex Genetic Testing Panels**

**Genetic tests that provide information about future risks for unrelated disorders should be included in multiplex testing panels only when they meet all criteria for genetic screening tests. Tests should be grouped based on similar issues and implications to allow for adequate counseling and consent. For tests to determine risks for late-onset diseases, tests placed in multiplex panels should provide a demonstrated, significant medical benefit and should be offered on an age-appropriate basis. For reproductive carrier testing, tests placed on a multiplex panel should be for diseases of similar seriousness.**

By bundling together predictive genetic tests to determine future risks for unrelated disorders, multiplex panels are, in effect, screening tests, and all tests on a multiplex panel should be subject to all requirements of screening tests. Each test placed on a multiplex panel must have adequate and confirmed analytical and clinical validity for the population to whom it is offered, as well as significant clinical utility.

The combined offering of multiple screening tests for unrelated disorders, however, raises additional concerns because of the difficulty of providing meaningful, detailed education and counseling about all possible test results. Questions thus emerge as to how tests should be bundled together to provide multiplex panels for which pretest education and meaningful consent are feasible. For susceptibility tests to determine relative risk for late-onset disorders for which the benefits of testing clearly outweigh risks, in the form of demonstrated medical or behavioral preventive interventions such that most individuals would agree to undergo screening if they were fully informed about each test, we agree that grouping of tests in a multiplex panel is acceptable.

In practice, however, there are likely to be significant variations among tests, even when limited to tests for a related set of disorders, such as cancers. Such tests can differ significantly in the degree of demonstrated clinical validity and clinical utility. We agree with the IOM Committee that tests that are offered together in a multiplex panel should raise similar issues and implications.[256] We also agree with them that further research in this area is needed, including research about how educational tools, including video and computer-based tools, might be helpful.

For genetic testing panels to detect an individual's future risks for late-onset disorders, factors to consider for construction of multiplex panels include degree of relative risk, degree of efficaciousness of a preventive intervention, age of onset, and type of disorder. For example, the implications of testing positive for a susceptibility mutation for mental disorders may differ from those associated with risk for cardiopulmonary

[256] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 275.

diseases or obesity. Tests should be grouped in multiplex panels so that they are offered to individuals at the time of their life (e.g., early versus late adulthood) when implementation of associated preventive interventions is required. Bundling by ethnic or racial background, while understandable at the present time, presents the risks of discrimination as well as missed risk diagnoses. In the future, the identification of susceptibility gene variants for different populations, along with development of cheaper and faster testing technologies such as the DNA chip, should permit screening for broader panels of mutations.

For testing of adults to determine future disease risks, limitations regarding meaningful education, pretest counseling, and consent for multiplex testing also raise the level of clinical utility that should be required for screening tests. When full counseling and informed consent for a particular test are available, an individual has the option to weigh the test's risks against the degree and kind of benefits the test may provide. Different individuals may make different choices based on the degree of medical benefit. When detailed informed consent for each disorder is not feasible, these types of decisions are not possible. This raises the bar for the required level of clinical utility of testing to counter potential harms based on testing results. For inclusion in a multiplex testing panel, the balance of benefits and risks should be such that most individuals would agree to testing if they were fully informed.

While late-onset disease panels will generally include susceptibility gene testing, existing reproductive multiplex screening panels offered to Ashkenazi Jewish individuals contain tests for single-gene disorders. The necessity of meaningful counseling, education, and consent for reproductive screening tests also is clear and requires that tests raise similar issues and implications. Tests might be grouped by type of morbidity (e.g., neurodegeneration), by whether they are for disorders with variable ranges of seriousness, and by whether or to what degree a medical treatment is available.

# 6

# Newborn Screening

Newborn screening was the first population-based screening program in the United States,[1] and it is the most widely performed type of genetic testing in the United States today.[2] State public health programs screen four million infants per year for a number of congenital conditions. [3] Generally, the goal of newborn screening is to detect infants affected by conditions for which prompt application of confirmed preventive interventions can prevent or reduce disease, disability, and/or death. Most conditions tested for are genetic disorders, generally autosomal recessive disorders that result from the absence of some critical enzyme activity.[4] An autosomal recessive disorder manifests when an infant inherits two mutated copies of a single gene, one from each parent; parents generally have no family history of the disorder.[5] States also screen for some nongenetic disorders, including congenital hypothyroidism and seropositivity for human immunodeficiency virus (HIV).[6]

## History of Newborn Screening

The first newborn screening test instituted in the United States was for detection of the metabolic disorder phenylketonuria (PKU).[7] PKU is caused by the absence of a specific enzyme that processes a dietary form of an amino acid (a protein building block)

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[1] American Academy of Pediatrics Newborn Screening Task Force (Newborn Screening Task Force), "Serving the Family from Birth to the Medical Home — Newborn Screening: A Blueprint for the Future," *Pediatrics* 106 (2000): 389.

[2] E. H. Hiller, G. Landenburger, and M. R. Natowicz, "Public Participation in Medical Policy Making and the Status of Consumer Autonomy: The Example of Newborn Screening Programs in the United States," *American Journal of Public Health* 87 (1997): 1280.

[3] Congenital conditions are conditions existing at birth, which may be of genetic or nongenetic origins. R. C. King and W. D. Stansfield, *A Dictionary of Genetics*, 5th ed. (New York: Oxford University Press, 1997), 79.

[4] When an infant inherits two mutant copies of a gene that "codes for" a particular enzyme, a deficiency in that enzyme results. Enzymes are proteins that convert one body substance (a substrate) into another component (a product). Absence of an enzyme results in an abnormal buildup of one or more substrates and/or a depletion of products. For further discussion, see Chapter 2, page 40.

[5] Carrier parents each have one mutant and one normal copy of the relevant gene. The presence of the normal gene copy is generally sufficient to prevent any health impairment in carriers. For discussion of autosomal recessive disorders, see Chapter 1, page 16.

[6] The causes of congenital hypothyroidism are not clearly defined; in some cases, genetic factors may contribute. The New York State Newborn Screening Program has tested for HIV seropositivity since 1997. See page 149, this chapter.

[7] See Chapter 2, page 40.

called phenylalanine. Failure to process dietary phenylalanine leads to an abnormal accumulation in the blood and tissues. Affected infants (approximately 1 in 12,000 births) appear normal at birth but, if untreated, become severely retarded in infancy or early childhood.[8]

In the early 1960s, researchers produced a dietary formula for those affected by PKU containing other protein building blocks but low in phenylalanine.[9] Shortly thereafter, Dr. Robert Guthrie developed a laboratory test to measure blood phenylalanine levels. Dr. Guthrie also established the procedure for obtaining the newborn specimen on a piece of filter paper, the "bloodspot" that is still used today. In this procedure, a row of tiny blood samples is spotted on a filter paper for each infant; they are obtained by a "heelstick," a relatively painless and risk-free procedure.[10]

In 1963, Massachusetts became the first state to establish a newborn PKU screening program. Nationally, the National Association of Retarded Children, an organization of professionals and parents of retarded children, proposed a model law to promote screening in other states and worked with officials of state public health departments. By 1975, forty-three states had enacted laws to establish newborn PKU screening; today all states and many countries outside the United States perform newborn PKU screening.[11]

When it was first introduced, both the American Medical Association (AMA) and the American Academy of Pediatrics (AAP) questioned newborn PKU screening on several grounds and initially opposed it.[12] A major concern was whether the test had adequate sensitivity (ability to detect all affected infants) and specificity (ability to exclude all children without the disorder). In fact, during the early years of PKU screening, some infants with PKU were not identified.[13] Others were incorrectly identified as PKU-positive and treated inappropriately, in some cases causing significant

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[8] M. R. Natowicz and J. S. Alper, "Genetic Screening: Triumphs, Problems, and Controversies," *Journal of Public Health Policy* 12 (1991): 475, 479.

[9] See D. B. Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," in National Institutes of Health-Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing in the United States*, ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of Health, 1997) 137, 138.

[10] See New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/footpix.htm*, visited May 27, 1999.

[11] Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 138.

[12] Ibid., 141–143; American Academy of Pediatrics, "Statement on Compulsory Testing of Newborn Infants for Hereditary Metabolic Disorders," *Pediatrics* 39 (1967): 623.

[13] See Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 142. The first systematic review of PKU testing, in 1974, reported that 10 percent of PKU-positive infants were not identified.

harm.[14] Even for correctly diagnosed PKU-positive children, questions remained about the effectiveness of the dietary treatment, the necessary duration of treatment, and the possibility of harms associated with overtreatment. In 1967, a United States Public Health Service Collaborative Study for Children Treated for PKU addressed these questions and established that the diet was adequate for normal growth and reduced the risk of severe retardation but required early implementation and strict maintenance, at least throughout childhood.[15] The testing problems (unacceptable false positive and false negative rates) also were addressed.[16] Today, PKU screening is widely used and represents "what many consider an ideal preventive health measure," preventing mental retardation in thousands of children.[17]

By the 1970s, states had begun to add tests for other disorders to their newborn screening programs. In response to lessons learned during implementation of PKU screening, the National Research Council (NRC) urged state legislatures to avoid "ad hoc responses to pleas for state involvement in the increasing number of conditions for which screening will become available."[18] Others emphasized the necessity of conducting pilot studies to confirm the value of testing prior to implementation of screening programs.[19] Despite warnings, many states implemented new tests without first establishing their clinical diagnostic value (clinical validity) and the existence of reliable treatment interventions for children who tested positive (clinical utility).[20] Examples included screening for histidinemia, a condition that does not cause symptoms or require treatment, and screening for cystic fibrosis in the absence of any confirmed benefit to the newborn.[21] In fact, only a minority of newborn screening tests that are currently performed have been

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[14] See ibid., 143; Natowicz and Alper, "Triumphs, Problems, and Controversies," 480; N. Fost, "Ethical Implications of Screening Asymptomatic Individuals," *FASEB Journal* 6 (1992): 2814. While high blood phenylalanine levels are characteristic of classical PKU, some infants with equally high levels may have milder or transient clinical syndromes that do not require or respond to treatment.

[15] See Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 144, 145. The diet is very restrictive and requires use of expensive supplements. The study was sponsored by the Children's Bureau of the Department of Health and Human Services (now the Maternal and Child Health Bureau).

[16] Significant reduction of the test's high false positive rate was achieved by retesting original screen test positive infants several weeks later. Dr. Paul Edelson, Columbia University College of Physicians and Surgeons, Center for Society and Medicine, presentation to the New York State Task Force on Life and the Law, January 14, 1998. The New York State Newborn Screening Program now performs immediate retesting of the original bloodspot with a more specific test, eliminating some false positive results without parental notification or a second visit to the doctor. Dr. Ken Pass, Director of the New York State Newborn Screening Program, presentation to the New York State Task Force on Life and the Law, April 30, 1999.

[17] President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions* (Washington, D.C.: U.S. Government Printing Office, 1983), 12–13.

[18] Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 147.

[19] President's Commission, *Screening and Counseling for Genetic Conditions*, 71.

[20] For a discussion of clinical validity and utility, see Chapter 2, page 41.

[21] N. A. Holtzman, "Editorial: Genetic Screening and Public Health," *American Journal of Public Health* 87 (1997): 1275; N. A. Holtzman, "What Drives Neonatal Screening Programs?" *New England Journal of Medicine* 325 (1991): 802, 803. More recently, debate about the clinical benefit of newborn cystic fibrosis testing has been re-opened. See page 159, this chapter.

demonstrated formally to have both clinical validity and utility.[22] These include tests to detect PKU and congenital hypothyroidism, for which immediate intervention can prevent mental retardation,[23] and sickle cell disease, for which prophylactic antibiotic treatment reduces early childhood mortality.[24]

Today, as a result of the Human Genome Project, genetic variations that underlie inherited disorders and the technology to detect them are expanding rapidly. These developments will present state screening programs with expanded lists of disorders for which testing is possible and with new testing methods. In addition to new DNA-based test development, a use of a technology called tandem mass spectrometry (TMS) is introducing a "sea change" in newborn screening.[25] TMS can detect twenty-five or more metabolic disorders from a newborn bloodspot in a single test. The American College of Medical Genetics (ACMG) estimates that this method could increase identification of infants affected with congenital metabolic disorders by 50 to 100 percent.[26] The extremely low false positive rates of this method also could reduce costs of confirmatory follow-up testing.[27]

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[22] Holtzman, "Genetic Screening and Public Health." See also M. J. Thomason et al., "A Systematic Review of Evidence for the Appropriateness of Neonatal Screening Programmes for Inborn Errors of Metabolism," *Journal of Public Health Medicine* 20 (1998): 331.

[23] Hypothyroidism is treated by administration of thyroid hormone supplements. See American Academy of Pediatrics Committee on Genetics, "Newborn Screening Fact Sheets," *Pediatrics* 83 (1989): 449, 454–455.

[24] See National Institutes of Health Consensus Conference, "Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies," *Journal of the American Medical Association* 258 (1987): 1205; see also Centers for Disease Control and Prevention, "Mortality among Children with Sickle Cell Disease Identified by Newborn Screening during 1990–1994 — California, Illinois, and New York," *Morbidity and Mortality Weekly Report* 47 (1998): 169.

[25] H. L. Levy, "Newborn Screening by Tandem Mass Spectrometry: A New Era," *Clinical Chemistry* 44 (1998): 2401. For a discussion of TMS, see Chapter 2, page 47.

[26] American College of Medical Genetics Test and Technology Transfer Committee, "ACMG Statement: Tandem Mass Spectrometry in Newborn Screening," 1999.

[27] Ibid.; Levy, "Tandem Mass Spectrometry: A New Era," 2401. Application of this method for PKU screening was reported to yield approximately 1 percent of the false positive results of traditional test methods. See D. H. Chace et al., "Use of Phenylalanine to Tyrosine Ratio Determined by Tandem Mass Spectrometry to Improve Newborn Screening for Phenylketonuria of Early Discharge Specimens during the First 24 Hours," *Clinical Chemistry* 44 (1998): 2404.

## Current Programs and Practice

### Overview of State Newborn Screening Programs

The United States has fifty-three newborn screening programs, one in each of the fifty states, the District of Columbia, Puerto Rico, and the Virgin Islands.[28] Most states have specific legislation that mandates newborn screening programs and provides authority, generally to the state health department, to add to or delete tests from the program.[29] Most state programs were established independently, and program characteristics and effectiveness vary widely.

Federal programs have provided both networking and financial support to the state newborn screening programs. The Maternal and Child Health Bureau (MCHB) of the Health Resources and Services Administration (HRSA) helped states establish their screening programs.[30] In the 1970s, in response to concerns about quality assurance issues for newborn screening tests and programs, the Centers for Disease Control and Prevention (CDC) established the Newborn Screening Quality Assurance Program.[31] Also, for almost fifteen years, the Council of Regional Networks for Genetic Services (CORN), a federally funded national forum for information exchange about public health genetic services, addressed newborn screening program issues and produced screening guidelines.[32] In 1999, in response to advancing genetic technologies and new issues in newborn screening, HRSA requested that the AAP convene a task force (the Newborn Screening Task Force) to develop multidisciplinary recommendations to advance newborn screening systems, with emphasis on the role of public health agencies, providers, and families.[33]

### Components of a Screening Program

In 1999, CORN described newborn screening as a "five part preventive health care system designed to identify and treat selected conditions that would otherwise become catastrophic health problems."[34] These five components, which show considerable overlap, are: (1) the screening test, (2) follow-up and reporting of positive screening test results, (3) diagnostic confirmation of a screen-positive newborn, (4) rapid implementation of a medical

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[28] B. L. Therrell, "Guidelines for Genetic Laboratory Practices: Newborn Screening," in *Genetic Services: Developing Guidelines for the Public's Health*, proceedings of a conference held in Washington, D.C., February 16–17, 1996, 185.

[29] Ibid., see also J. J. Stoddard and P. M. Farrell, "State-to-State Variations in Newborn Screening Policies," *Archives of Adolescent and Pediatric Medicine* 151 (1997): 561; L. B. Andrews, *State Laws and Regulations Governing Newborn Screening* (Chicago: American Bar Association, 1985), 1–18.

[30] See Council of Regional Networks for Genetics Services, *U.S. Newborn Screening System Guidelines II: Follow-up of Children, Diagnosis, Management, and Evaluation* (Atlanta: CORN, March 1999), 9. See also Newborn Screening Task Force, "A Blueprint for the Future," 390.

[31] See Newborn Screening Task Force, "A Blueprint for the Future," 390.

[32] See Council of Regional Networks for Genetic Services, website: *http://www.cc.emory.edu/PEDIATRICS/corn/office/mission.htm*, visited February 2, 1999. CORN was established in 1985. See B. L. Therrell et al., "U.S. Newborn Screening System Guidelines: Statement of the Council of Regional Networks for Genetic Services," *Screening* 1 (1992): 135.

[33] Newborn Screening Task Force, "A Blueprint for the Future."

[34] Council of Regional Networks for Genetic Services, *Follow-up of Children*, 11.

intervention and planning for long-term care, and (5) periodic program evaluation to assess validation of test procedures and for "assessment of the benefit to patient, family, and society."[35]

### *Screening Tests*

Most state programs have assembled their screening test panels over several decades without formal criteria or processes to guide the addition of new tests.[36] All states test for PKU and hypothyroidism, and most test for sickle cell disease and a variable mix of additional disorders.[37] Most, but not all, programs use centralized testing facilities.[38] Some states authorize the use of designated testing laboratories.

Newborn screening tests in most programs are universal; that is, all newborns are screened for each disorder. Some programs, however, target screening for hemoglobinopathies (sickle cell disease and thalassemia) to minority populations that are perceived to be at higher risk than the general population.[39] Some commentators claim that targeted screening imposes a burden on parents and health care providers to correctly identify ethnic or racial background and increases the chance of missed diagnoses.[40]

### *Follow-up of Presumptive Positive Test Results*

Newborn screening tests are designed for maximal sensitivity (detecting every true positive), often at the expense of specificity (resulting in false positive results).[41] As a result,

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[35] Ibid.

[36] B. S. Wilfond and K. Nolan, "National Policy Development for the Clinical Application of Genetic Diagnostic Technologies: Lessons from Cystic Fibrosis," *Journal of the American Medical Association* 270 (1993): 2948, 2949.

[37] Hiller, Landenberger, and Natowicz, "Public Participation in Medical Policy Making," 1282. Some programs may have changed their screening panels subsequent to this survey. For an updated listing, see Newborn Screening Task Force, "A Blueprint for the Future," 393. For a description of the disorders screened for and testing methods and issues, see E. R. Brown, "Metabolic Screening," *Clinics in Perinatology* 25 (1998): 37; see also American Academy of Pediatrics Committee on Genetics, "Newborn Screening Fact Sheets," September 1996, American Academy of Pediatrics website: *http://www.aap.org/policy/01565.html*, visited February 10, 1999.

[38] Newborn Screening Committee, Council of Regional Networks for Genetic Services, *National Newborn Screening Report — 1994*, (Atlanta: CORN, 1999), 26.

[39] Newborn Screening Task Force, "A Blueprint for the Future," 392–393; D. Wertz, "Newborn Screening: State Policies on Testing, Informed Consent, and Public Input," *The Gene Letter* (March 1998), website: *http:// www.geneletter.org*, visited June 2, 1998.

[40] Wertz, "Newborn Screening: State Policies on Testing, Informed Consent, and Public Input."

[41] See C. Kwon and P. M. Farrell, "The Magnitude and Challenge of False-Positive Newborn Screening Test Results," *Archives of Pediatric and Adolescent Medicine* 154 (2000): 714.

samples that test positive in an initial screening test must be retested using a more specific, and generally more expensive, follow-up test. Accurate and timely follow-up testing is critical to ensure appropriate identification and treatment of affected infants and to minimize parental anxiety associated with uncertain or worrisome test results.

In some cases, the screening program may retest the original bloodspot of a presumptive screen test positive infant using a more specific confirmatory test for the same disorder. This can spare parents the anxiety associated with notification and follow-up of a newborn with a false positive result. If a new blood sample is required, it is essential that there be a rapid and reliable method of contacting physicians to ensure prompt testing and follow-up. Physicians, aided by newborn screening personnel, should be able to explain the need for follow-up testing to parents without causing unwarranted anxiety.

### *Diagnosis of Affected Newborns*

Commentators agree that newborn screening programs should ensure follow-up of any positive test result, including prompt diagnostic assessment by appropriate specialty care providers.[42] Programs need to ensure that potentially affected infants are not "lost to follow-up" when parents do not come in for initial appointments at clinical specialty centers.[43] Programs also should ensure counseling for parents of newborns identified to have disorders.[44] Forty-three state screening programs reported that they had statutes, regulations, and/or policies to specify protocols for follow-up of infants whose screening tests are positive, but these vary widely.[45]

### *Management of Care*

Newborns diagnosed positive for a screened disorder should be referred to appropriate centers and to providers who can initiate care and develop a long-term care plan. The Newborn Screening Task Force endorsed the concept of establishing a "medical home" in which a child receives "accessible, continuous, comprehensive, family centered, coordinated, and compassionate care"[46] from a physician known to the child and family.[47] CORN and the Newborn Screening Task Force both stated that state

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[42] Therrell et al., "U.S. Newborn Screening Guidelines," 139, 140; American Academy of Pediatrics, "Issues in Newborn Screening," *Pediatrics* 89 (1992): 345, 347; Council of Regional Networks for Genetic Services, *Follow-up of Children*, 15, 31; American College of Medical Genetics, "Principles of Screening: Subcommittee of the American College of Medical Genetics Clinical Practice Committee" (February 28, 1997), American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/policy/pol.26.htm*, visited February 22, 1999.

[43] See, e.g., S. T. Miller et al., "Newborn Screening for Sickle Cell Disease: When Is an Infant Lost to Follow-up?" *American Journal of Diseases of Childhood* 144 (1990): 1343.

[44] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 6.

[45] Hiller, Landenberger, and Natowicz, "Public Participation in Medical Policy Making," 1281, 1282.

[46] American Academy of Pediatrics, Policy Statement RE9262, "The Medical Home," *Pediatrics* 90 (1992), 774.

[47] Newborn Screening Task Force, "A Blueprint for the Future," 386, 395.

newborn screening programs should identify appropriate specialty care physicians and centers.[48]

CORN's guidelines outline appropriate patient management approaches for the major disorders detected by newborn screening tests. For example, for sickle cell disease, the guidelines state that treatment to ensure optimal outcome requires the active involvement of a pediatric hematologist as well as professionals in nursing, social work, psychology, genetics, education, and counseling. They state that "when such teams are not available locally, ongoing input from sickle cell experts should be obtained."[49] In recent years, some commentators have expressed concerns that the changing health care infrastructure, dominated by managed care plans, has reduced the likelihood that individuals with sickle cell disease will receive appropriate specialist care.[50]

Another concern is the financial ability of families with affected children to pay for long-term medical care, which is often expensive. The Institute of Medicine Committee on Assessing Genetic Risks (IOM Committee) stated that treatment of newborns who test positive should be ensured, without regard to ability to pay.[51] Others agree that screening programs bear a responsibility to ensure access to continuous care by coordination of state referral services and social insurance programs.[52] States may designate affected newborns as eligible for government administered programs. For metabolic disorders such as PKU, dietary supplements are an expensive and necessary component of care that is not always covered by insurers.[53] Some states require by law that private insurance companies provide coverage for nutritional supplements for children with metabolic disorders, but self-funded employer-based benefit plans are not covered by state insurance mandates.[54] The Newborn Screening Task Force recommended that states should require that all health plans, including publicly subsidized managed care plans, provide the services outlined in CORN newborn screening guidelines.[55]

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[48] Ibid.; Council of Regional Networks for Genetic Services, *Follow-up of Children*, 57.
[49] Council of Regional Networks for Genetic Services, *Follow-up of Children*, 57.
[50] J. H. Bilenker et al., "The Costs of Children with Sickle Cell Anemia: Preparing for Managed Care," *Journal of Pediatric Hematology/Oncology* 20 (1998): 528; comments by parents and providers at the Genetics Network of New York, Puerto Rico and the Virgin Islands (GENES) Sickle Cell Advisory Committee Meeting, New York City, January 26, 2000.
[51] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 5–6.
[52] See Newborn Screening Task Force, "A Blueprint for the Future," 395.
[53] The PKU dietary formula was originally classified as a drug, and children were generally taken off the diet by age five or six. In 1972, the formula was reclassified as a food, reportedly causing many insurers to stop reimbursement for it. Also, persons with PKU were advised to maintain the diet into adulthood. Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 145. See also National PKU News website: *http://www.wolfenet.com*, visited May 27, 1999.
[54] National PKU News website: *http://www.wolfenet.com*.
[55] Newborn Screening Task Force, "A Blueprint for the Future," 394.

### *Program Evaluation*

Evaluation consists of validation of a program's testing procedures, assessment of the efficiency of follow-up and intervention, and assessment of the benefit to the patient, family, and society. This evaluation requires continuous data collection and analysis. CORN's guidelines outline essential data that are needed to ensure effective screening and to promote integration of program data with other data sources, for example, birth records and treatment center records.[56] The evaluation of long-term health outcomes of newborns identified to have a disorder is one of the most important and difficult components to evaluate, and it requires input from all program components as well as community health care providers. Some states maintain long-term follow-up of individuals identified to have PKU, sickle cell disease, or other disorders.[57] It is critical that data collection and evaluation are subject to appropriate confidentiality protections. The Newborn Screening Task Force emphasized the responsibility of state programs "to ensure quality and evaluation program effort" and recommended that federal resources assist the state programs in these efforts.[58]

## New York State's Newborn Screening Program

In 1965, New York State enacted legislation establishing newborn screening for PKU.[59] The law also gave the Commissioner of Health discretionary powers to designate screening for other diseases and conditions. Since 1965, amendments to the law (and/or regulations)[60] have added screening for the following congenital disorders: branched chain ketonuria, homocystinuria, galactosemia, hemeglobinopathies (including sickle cell disease),[61] hypothyroidism, HIV seropositivity, and biotidinase deficiency.[62] The frequency of affected newborns for each disorder varies, from more than 1 in 500 for HIV seropositivity to approximately 1 in 225,000 for homocysteinuria.[63] Annually, over 250,000 newborns are screened in New York, and over 500 are diagnosed with congenital

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[56] Council of Regional Networks for Genetic Services, *Follow-up of Children*.

[57] See Council of Regional Networks for Genetic Services, *National Newborn Screening Report — 1994*, 27.

[58] Newborn Screening Task Force, "A Blueprint for the Future," 387.

[59] N.Y. Pub. Health Law § 2500-a (McKinney 1999).

[60] New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/index.htm*, visited January 28, 1999. The law was amended to add new tests (or, in one case, to delete a test) in 1968, 1975, 1978, 1986, and 1997. Screening for biotidinase deficiency is stipulated by regulations only. 10 N.Y.C.R.R. § 69-1.2(b)(2000).

[61] The law specifies testing for "homozygous sickle cell disease," but the program also screens for additional hemoglobinopathies.

[62] In 1997, HIV seropositivity newborn screening was mandated. N.Y. Pub. Health Law § 2500-f (McKinney 1999). The screening test detects antibodies to HIV, which indicate infant exposure to maternal HIV infection. About one-quarter of infants who test positive will develop HIV infection and may benefit from early detection and treatment. New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/index.htm*, visited January 28, 1999.

[63] New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/disorders.htm*; *http://www.wadsworth.org/newborn/annualrpt/nbs97.htm*, visited March 31, 1999; *http://www.wadsworth.org/newborn/annualrpt/nbs98.htm*, visited May 27, 1999.

disorders, excluding HIV seropositivity.[64] In recent years, approximately 800 HIV seropositive infants have been identified annually.[65]

## Screening, Follow-up, and Diagnosis

Newborn blood samples are obtained at hospitals using the bloodspot method pioneered by Dr. Guthrie in 1962.[66] Hospitals send the samples to a centralized testing laboratory at the New York State Department of Health. Before hospital discharge, mothers receive a form that tells them that their baby has been tested and encourages them to ask their pediatrician for test results. Samples determined to be positive in the initial screening test are immediately retested, usually by a different, more specific method. This eliminates many, but not all, false positive results before physicians and parents are notified. For example, a confirmatory follow-up for PKU reduces the number of presumptive positive infants (and number of notified parents) by 80 percent.[67]

The program reports results to designated licensed physicians and the hospital of birth. In addition, the program has implemented an automated, password-protected telephone system that allows physicians to phone in to confirm receipt of a sample and to learn the testing status and results.[68] For infants presumed positive based on both the initial screen and the follow-up test, the program requests a repeat specimen and, as appropriate, directs newborns for clinical evaluation. New York's Genetics Services Program refers screen-positive newborns to designated comprehensive genetic service centers for definitive diagnostic evaluation, regardless of ability to pay. [69]

### *Management of Care*

The New York State Department of Health ensures the existence of accessible specialized treatment centers and departmental programs to help families access coverage for the special health care needs of their children. For example, the Children with Special Health Care Needs Program helps link families to federal, state, and county-based social

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[64] New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/annualrpt/nbs98.htm*.
[65] Ibid.
[66] See page 142, this chapter.
[67] Dr. Ken Pass, Director of the New York State Newborn Screening Program, presentation to the New York State Task Force on Life and the Law, April 30, 1999.
[68] The system uses a toll-free number and is available to New York State-licensed physicians who register with the New York State Department of Health and obtain a security-protected password. In October 1997, approximately 6,000 calls were received to obtain 49,000 results. Dr. Ken Pass, Director of the New York State Newborn Screening Program, presentation to the New York State Task Force on Life and the Law, January 14, 1998.
[69] 10 N.Y.C.R.R. § 69-1.7 (1997).

insurance programs, including Child Health Plus,[70] Medicaid, and the Physically Handicapped Children's Program.[71] The department's Genetics Services Program and other partners within the state are working to produce guidelines to ensure that managed care organizations and their health care providers make appropriate referrals for children with sickle cell disease to specialty care providers and centers.[72]

One important component of long-term care for individuals with PKU or other metabolic disorders is the use of expensive dietary supplements. New York law requires that health insurance policies that provide coverage for prescription drugs provide coverage of

dietary formulas and supplements essential to nutritional therapy for PKU and related metabolic disorders.[73]

### *Program Evaluation*

New York's Newborn Screening Program produces an annual report containing data for the number of infants screened, those identified as presumptive positive by screening, and those confirmed diagnostically to have a disorder.[74] The program does not have any additional formal evaluation process, and there is no systematic follow-up of newborns who test positive for disorders such as PKU or sickle cell disease. In a 1998 multistate study to assess medical follow-up of infants identified to have sickle cell disease in 1992 and 1993, New York could confirm ongoing receipt of appropriate care for less than 40 percent of identified children.[75]

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[70] See P. G. Szilagyi et al., "Evaluation of a State Insurance Program for Low-Income Children: Implications for State Child Health Insurance Programs," *Pediatrics* 105 (2000): 363; see also New York State Department of Health website: *http://www.health.state.ny.us/nysdoh/chplus/brochure.htm*, visited November 3, 1999. The program covers a range of preventive and specialized care for children under the age of nineteen who are uninsured and not eligible for Medicaid. Premiums are subsidized based on family income. In New York State, more than 435,000 children are enrolled. See also "Commissioner Novello Leads Child Health Plus Enrollment Day — Governor Pataki's Commitment to Child Health Plus Makes It Nation's Best Program," *http://www.health.state.ny.us/nysdoh/commish/2000/enroll.htm*, visited February 25, 2000.

[71] See New York State Department of Health Resource Directory for Children with Special Health Care Needs, New York State Department of Health website: *http://www.health.state.ny.us/nysdoh/prevent/special/special.htm*, visited February 25, 2000.

[72] Telephone interview with Katharine Harris, New York State Department of Health Genetics Services Program Coordinator, June 11, 1999.

[73] N.Y. Insurance Law § 3216 (McKinney 1999). The law specifies coverage for enteral formulas that are prescribed by a physician or other licensed health care provider for specified disorders. Coverage for certain metabolic disorders also includes modified solid food products for up to $2,500 per year.

[74] See, e.g., New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/annualrept/nbsrpt98.htm*.

[75] K. Pass et al., "Update: Newborn Screening for Sickle Cell Disease — California, Illinois, and New York, 1998," *Morbidity and Mortality Weekly Report* 49, no. 32 (2000): 729.

## Newborn Screening Program Issues

### *Parental Consent to Newborn Screening*

In all states except Maryland and Wyoming, parental consent is not required for newborn screening.[76] Thirty-three programs only permit religious objections to screening, while seventeen programs allow parental refusal for religious and/or personal reasons.[77] For states that allow some form of parental refusal, only thirteen require that parents be informed of screening and provided with educational materials prior to testing.[78]

New York does not require parental consent to newborn screening.[79] Although the law allows parental refusal of testing on religious grounds, many parents are not informed of their right to object.[80] Although New York's Newborn Screening Program produces brochures to inform parents about screening[81] and the program sends brochures to hospitals and other institutions of birth for distribution to parents, many parents do not receive these brochures until after testing has begun.[82]

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[76] Hiller, Landenburger, and Natowicz, "Public Participation in Medical Policy Making," 1283. Also, Georgia requires written informed consent only for hemoglobinopathy screening targeted to individuals based on racial or ethnic groups. In Maryland, the law states that each participant shall be informed of the nature, costs, benefits, and risks of therapy or maintenance programs available to an affected individual. Md. Public Health Code Ann. § 13-109 (g)(1)(ii) (1982). In 1999, Massachusetts began using informed "dissent" for pilot testing of investigational stage newborn screening tests. See page 166, this chapter.

[77] Hiller, Landenburger, and Natowicz, "Public Participation in Medical Policy Making," 1281.

[78] Ibid. California, Wisconsin, and the District of Columbia require that parents be given a reasonable opportunity to object to newborn screening.

[79] New York regulations also require and do not allow exemptions based on parental objections for two other prophylactic treatments of newborns performed at hospitals, vitamin K injection and eye prophylaxis. N.Y.C.R.R. § 12.2 and 405.21 (e)(4)(v)(b). Both treatment measures are recognized as the standard of care for newborns. American Academy of Pediatrics, *Guidelines for Perinatal Care*, 4th ed. (Washington, D.C.: American Academy of Pediatrics, 1997).

[80] N.Y. Pub. Health Law § 2500-a(b) (McKinney 1999). The law states that the requirement for screening "shall not apply in the case of any infant whose parent or guardian is a member of a recognized religious organization where teachings and tenets are contrary to the testing herein required and who notifies the person charged with having such test administered of his objection thereto."

[81] Brochures in English, Spanish, and French are provided to hospitals and other birth institutions and also are available to consumers on the New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/order.htm*, visited March 31, 1999.

[82] Current regulations require the New York State Department of Health Wadsworth Center to "provide educational activities and materials" but do not stipulate to whom materials should be provided (10 N.Y.C.R.R. § 69-1.8). Another section of the regulations requires the chief executive officer of the hospital or institution of birth to see that "the infant's parent is informed of the purpose and need for newborn screening and given educational materials provided by the testing laboratory" (10 N.Y.C.R.R. § 69-1.3).

Screening without parental consent has been justified on the basis of the state's *parens patriae* power, which permits the state to intervene to protect children from substantial and imminent harm.[83] Many commentators and policy groups have accepted this rationale, provided that testing has both demonstrated validity and strong evidence of benefits to the infants tested.[84] In 1997, the Task Force on Genetic Testing of the National Institutes of Health-Department of Energy Working Group of the Ethical, Legal and Social Implications of Human Genome Research (the NIH-DOE Task Force on Genetic Testing) added that parents also must be provided with sufficient information to understand the reasons for testing.[85] One commentator points out, however, that some tests on state screening panels fall short of the levels of demonstrated clinical validity and utility espoused by the NIH-DOE Task Force on Genetic Testing.[86]

Some commentators disagree with state exercise of *parens patriae* power for newborn screening. The IOM Committee stated that while it is appropriate to mandate the offering of newborn screening tests, informed consent should be an integral part of newborn screening.[87] They noted that informing parents about screening is an opportunity for public education about genetics and may provide the necessary understanding and motivation that will be needed for infants requiring follow-up.[88.]

Some commentators contend that the low population incidence of the disorders tested for (and low probability that any particular child will test positive) undermines the rationale for screening without parental consent.[89] Also, the Newborn Screening Task Force noted that overriding parental consent to screening in favor of preventing harms to the child "does not practically seem to be the basis of the current approach" taken by most states, since they generally allow for parental refusal under some circumstances.[90] They concluded that although written documentation of parental consent should not be required, "parents should always be informed of testing and have the opportunity to

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[83] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 261.

[84] R. R. Faden, N. A. Holtzman, and J. Chwalow, "Parental Rights, Child Welfare, and Public Health: The Case of PKU Screening," *American Journal of Public Health* 72 (1982): 1396; President's Commission, *Screening and Counseling for Genetic Conditions*, 6; NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 12; Consumers and Providers in the New England Regional Genetics Group, "Optimizing Genetics Services in a Social, Ethical, and Policy Context," *The Genetic Resource* 10, no. 2 (1996): 29.

[85] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 12.

[86] Holtzman, "Genetic Screening and Public Health," 1275.

[87] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 6. The committee later stated, however, that "mandatory newborn screening should only be undertaken if there is strong evidence of benefit to the newborn from effective treatment at the earliest possible age (e.g., PKU and congenital hypothyroidism)." Ibid., 262.

[88.] Ibid., 262.

[89] E. W. Clayton, "Screening and Treatment of Newborns," *Houston Law Review* 29 (1992): 85, 134, 146; G. J. Annas, "Mandatory PKU Screening: Through the Looking Glass," *American Journal of Public Health* 72 (1982): 1401. Annas states that the overriding "prevention of harm principle" should not be uncritically applied in a whole population scenario and that "the screening scenario is quite different from the dying child scenario."

[90] Newborn Screening Task Force, "A Blueprint for the Future," 410.

refuse testing."[91] They also concluded that documented consent should be required for investigational tests for which the benefits or potential risks of testing have not been fully demonstrated.[92]

### *Newborn Screening Advisory Committees*

The processes and criteria used to revise states' newborn screening test panels vary considerably.[93] In a 1997 survey of state newborn screening programs, thirty-six states reported that they had or were establishing an advisory committee for periodic review of their screening test panels.[94] The committees vary in whether they have policy-making authority or serve only in an advisory capacity. Committee composition also varies; some, but not all, include community representatives who are not health professionals. A minority of states reported that they convene advisory groups on an ad hoc basis or engage consultants as needed.[95] Fifteen states reported using institutional review boards (IRBs) to review activities associated with the newborn screening program, such as establishment of pilot programs for new tests. New York's Newborn Screening Program does not have a formal process to consider changes to the screening test panel and does not utilize an IRB or a formal advisory panel to consider the addition of new tests, although the program is reportedly considering establishment of such processes.[96]

The IOM Committee concluded that, historically, new tests have been added to state newborn screening panels without careful assessment of benefits and risks, often without the review of IRBs or other advisory groups.[97] Others state that the composition of screening test panels have not been determined rationally and are overly subject to the views of individual program personnel, other professionals, and advocacy groups.[98] To address this concern, the IOM Committee recommended that states form broadly representative, independent advisory bodies to guide health departments and legislatures on issues such as when new tests should be added and to ensure adequate counseling, education, and program evaluation.[99] The Newborn Screening Task Force and others

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[91] Ibid., 411.
[92] Ibid.
[93] See page 145, this chapter.
[94] Hiller, Landenberger, and Natowicz, "Public Participation in Medical Policy Making," 1283. In thirteen of these states, the advisory committees are required by law or regulation.
[95] Ibid. Seven states reported use of ad hoc committees, and five states reported use of consultants.
[96] Dr. Kenneth Pass, Director of the New York State Newborn Screening Program, June 4, 2000, personal communication.
[97] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 66–67.
[98] See, e.g., Holtzman, "What Drives Neonatal Screening Programs?" 802, 803; Wilfond and Nolan, "Lessons from Cystic Fibrosis," 2948, 2949.
[99] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 5, 294; American College of Medical Genetics, "Principles of Screening."

have also recommended that each state should establish a newborn screening advisory committee.[100]

Many commentators emphasize the importance of community representation in advisory bodies, noting that consumers are qualified to contribute to the nontechnical aspects of decisions and are the ones who bear the risks, as well as benefits, of screening programs.[101]

### *Financing of Newborn Screening*

CORN stated that program funding is the most difficult problem facing newborn screening programs.[102] In one survey of newborn screening programs, a chief obstacle to the addition of new screening tests to state panels was limited financial resources.[103] Programs vary in funding sources and covered activities. About 75 percent of newborn screening programs are funded through a fee-for-service, charging fees to patients, physicians, hospitals, or third-party payers.[104] Testing fees generally cover laboratory testing and program administration, and some also cover follow-up and diagnosis of newborns with positive screening test results.[105] The Newborn Screening Task Force stated that newborn screening fees and, if necessary, other public health funds should be used to ensure adequate funding for laboratory testing, diagnosis, and short-term follow-up of newborns.[106]

New York's Newborn Screening Program does not charge a screening fee.[107] The program uses state and federal funds but, in recent years, has lacked adequate funds to implement new screening tests, including testing to detect congenital adrenal hyperplasia, a disorder affecting 1 in 12,000 newborns for which established preventive interventions

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[100] Newborn Screening Task Force, "A Blueprint for the Future," 411; Therrell et al., "U.S. Newborn Screening System Guidelines," 137; Hiller, Landenberger, and Natowicz, "Public Participation in Medical Policy Making," 1288; Stoddard and Farrell, "State-to-State Variations," 561, 564; Wilfond and Nolan, "Lessons from Cystic Fibrosis," 2592–2593.

[101] Council of Regional Networks for Genetic Services, *Newborn Screening System Guidelines* (Phoenix: Council of Regional Networks for Genetic Services, 1990); Newborn Screening Task Force, "A Blueprint for the Future," 411; Hiller, Landenberger, and Natowicz, "Public Participation in Medical Policy Making," 1280–1283. For example, five of eleven voting members of the Maryland State Advisory Council on Hereditary and Congenital Disorders must not be health care providers or associated with health care institutions.

[102] Therrell et al., "U.S. Newborn Screening System Guidelines," 143.

[103] Stoddard and Farrell, "State-to-State Variations," 562.

[104] Therrell, "Guidelines for Genetic Laboratory Practices," 185; see also Council of Regional Networks for Genetic Services, *National Newborn Screening Report — 1994*, 29. In 1994, 39 programs charged fees, ranging from $10 to $59; the majority of program fees were $25 or less. See also Newborn Screening Task Force, "A Blueprint for the Future," 420–421.

[105] Council of Regional Networks for Genetic Services and Great Lakes Regional Genetics Group, *An Overview of Newborn Screening Programs in the United States, Canada, Puerto Rico and the Virgin Islands* (Atlanta: CORN, 1996), 2–3.

[106] Newborn Screening Task Force, "A Blueprint for the Future," 422.

[107] New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/newborn/babhealth.htm*, visited January 28, 1999.

exist.[108] In May 2000, a state budget directive allocated $5 million to the Newborn Screening Program.[109]

### *Storage and Research Use of Newborn Blood Samples*

After completion of the screening tests, residual sample material usually remains. Some programs destroy residual samples within a year of testing, but others retain samples for longer periods, in some cases for decades.[110] Samples are retained for different reasons, including legal accountability, laboratory quality control, and epidemiologic research to benefit the public health.[111] Newborn screening programs receive requests for both identified and anonymized bloodspots for research from within and outside the health agency.[112] The development of polymerase chain reaction (PCR) technology, allowing up to hundreds of genetics tests from individual stored newborn bloodspots, has contributed to program retention of samples for research purposes.[113] In addition to storing identified samples, some programs also anonymize samples by stripping identifying information and retain them in this form. CORN and the Newborn Screening Task Force recommended that programs define the rationale for retaining identified and anonymized samples and promulgate rules for sample retention and use.[114]

Newborn bloodspot collections provide a potentially valuable research resource of identified, coded, or anonymized samples.[115] However, as with research use of other samples obtained in the clinical context, research use of these samples raises concerns about confidentiality protections for sample sources and about group harms to, for example, racial and ethnic groups who are the subject of the research.[116] Some claim that ethical concerns about the use of newborn samples may be greater than for other samples

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[108] Dr. Ken Pass, Director of the New York State Newborn Screening Program, personal communication. The disorder results in ambiguity of sexual genitalia and risk of sudden death and is treated by administration of steroid hormones. See Thomason et al., "A Systematic Review of Evidence for the Appropriateness of Neonatal Screening Programmes," 338; American Academy of Pediatrics, "Newborn Screening Fact Sheets," 1996.

[109] New York State Governor's Budgetary Directive, S. 6404-B, enacted May 15, 2000.

[110] B. L. Therrell et al., "Guidelines for the Retention, Storage, and Use of Residual Dried Blood Spot Samples after Newborn Screening Analysis: Statement of the Council of Regional Networks for Genetic Services," *Biochemical and Molecular Medicine* 57 (1996): 116, 117; see also Newborn Screening Task Force, "A Blueprint for the Future," 414–415.

[111] For a discussion of epidemiologic research, see Chapter 11, page 314.

[112] Programs receive requests for sample collections and for individual identified samples, e.g., in cases where an infant dies of sudden infant death syndrome. Therrell et al., "Guidelines for the Retention, Storage, and Use of Residual Dried Bloodspot Samples," 122.

[113] For discussion of PCR, see Chapter 2, page 34.

[114] Therrell et al., "Guidelines for the Retention, Storage, and Use of Residual Dried Bloodspot Samples," 122; Newborn Screening Task Force, "A Blueprint for the Future," 415, 417.

[115] For a discussion of identified, coded, and anonymized samples, see Chapter 7, page 194.

[116] See Chapter 7, page 196; see also page 164, this chapter.

because mandatory screening programs collect them "as a matter of law."[117] Potential research use of these samples raises questions about the need for IRB review of research protocols and about whether programs should notify, or seek informed consent from, parents of newborns.

Several policy and professional groups have considered these questions. The IOM Committee recommended that newborn bloodspots should be made available for research "only if identifiers have been removed."[118] They also recommended that all research protocols using newborn bloodspots be approved by an IRB.[119] CORN stated that "anonymity appears to negate the need for obtaining parental consent since no possible physical or psychological harm to the parents or child could result and because the sample can provide population data that is important in public health studies."[120] They also noted that these samples are "limited and finite" and that requests for sample use should be limited to research that contributes to public or family health.[121] The Newborn Screening Task Force agreed that parental written consent for use of anonymized bloodspots should not be required for research that is "consistent with the goals of newborn screening."[122] However, they recommended that parents be informed about the potential use of residual anonymized bloodspots for quality assurance or epidemiologic research.[123] They also stated that protocols for the use of unidentified samples need not be submitted for IRB review.[124]

Commentators also have discussed criteria for use of identified newborn samples for research. The Newborn Screening Task Force stated that researchers requesting identified and coded samples should show that use of anonymized samples will not suffice, that newborn samples are the optimal tissue source for the research, and that acceptable samples from consenting adults are not available.[125] They also stipulated requirements for IRB approval of the research protocol and informed consent of parents.[126] They added that "in accordance with current federal regulations regarding research involving children, use of such samples for research, that poses more than minimal risk, should be limited to activities that benefit the child or that are important to understanding a condition affecting children."[127]

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[117] Newborn Screening Task Force, "A Blueprint for the Future," 415.
[118] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 6.
[119] Ibid.
[120] Therrell et al., "Guidelines for the Retention, Storage, and Use of Residual Dried Bloodspot Samples," 122.
[121] Ibid.
[122] Newborn Screening Task Force, "A Blueprint for the Future," 416.
[123] Ibid.
[124] Ibid.
[125] Ibid.
[126] Ibid.
[127] Ibid., 416–417.

New York's program has no formal policy for the retention of identified newborn bloodspots. In practice, samples are generally retained for six to nine months.[128] The New York State Department of Health has established a molecular genetic epidemiology laboratory that uses some residual bloodspots for public health research.[129] For use of identified or coded samples, limited to research within the department, the program recontacts parents for informed consent and requires IRB review.[130] In some cases, the Newborn Screening Program also provides anonymized samples for researchers outside the New York State Department of Health.[131]

### *Disclosure of Carrier Status*

Hemoglobinopathy screening detects not only homozygous, affected infants. It also detects an additional forty-fold newborns that are healthy carriers of a single mutant beta globin gene.[132] The information is not of direct benefit to the infant but can alert parents to their future reproductive risk.[133] Some programs provide carrier status information to providers and parents, while others do not. In New York's program, when hemoglobinopathy testing identifies carrier status in healthy infants, these results are reported to physicians. The physician has an opportunity to counsel parents about the infant's carrier status and its implications for the parents' future reproductive plans. However, at specialized care centers and state-supported genetic service providers,[134] where approximately 3,000 of 10,000 carrier infants identified annually are seen, physicians are required to counsel parents about their child's carrier status.[135]

The IOM Committee stated that newborn screening should not be performed for the *purpose* of detecting carrier status.[136] They concluded that when a newborn's carrier status is discovered as a by-product of a test to detect the disorder, it is not clear whether the benefits of informing parents about the infant's carrier status outweigh the risks. They suggested that the availability of adequate counseling services to help parents understand test results might be an important factor in resolving this dilemma.[137] CORN

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[128] Dr. Ken Pass, Director of the New York State Newborn Screening Program, presentation to the New York State Task Force on Life and the Law, April 30, 1999.
[129] Ibid. Disease-associated gene variants tested for include those associated with sickle cell disease and hemochromotosis.
[130] Dr. Ken Pass, Director of the New York State Newborn Screening Program, personal communication.
[131] Ibid.
[132] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 67; see also Chapter 5, page 114.
[133] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 67–70.
[134] See page 150, this chapter.
[135] Dr. Ken Pass, Director of the New York State Newborn Screening Program, presentation to the New York State Task Force on Life and the Law, January 14, 1998, and personal communication.
[136] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 67–70.
[137] Ibid.

guidelines recommend that a mechanism should be in place to notify parents about their newborn's carrier status and its meanings.[138] One commentator agrees, stating that "to ignore carriers is to miss undetected sickle cell disease in other members of the family or their future children."[139]

Future newborn screening panels may include additional tests, for example, cystic fibrosis testing, that also incidentally disclose carrier status.[140] Some opine that it may not be feasible, based on costs and limited resources, to notify and counsel parents about these results.[141]

## Benefits and Risks of Newborn Screening

### Benefits of Newborn Screening

#### *Reduced Morbidity and Mortality*

For some genetic conditions detectable by newborn screening, the benefits of reduced morbidity and mortality of identified infants are clear. For example, dietary therapy for infants with PKU can prevent the progress to severe mental retardation that would otherwise develop.[142] For infants identified as hypothyroid, administration of thyroid hormone can prevent severe retardation and other symptoms.[143] For children with sickle cell disease, prophylactic antibiotic therapy significantly reduces the incidence of life-threatening infections.[144]

#### *Alerting Parents to Future Reproductive Risks*

Another potential, but indirect, benefit exists for some newborn tests — the information that a newborn has a disorder resulting from inheritance of paired mutant genes from both parents or is a healthy carrier of a single recessive gene mutation (e.g., for sickle cell disease) may alert parents to future reproductive risks.[145] This information provides no immediate benefit to tested infants, but it may lead couples to undergo counseling and carrier

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[138] Council of Regional Networks for Genetic Services, *Guidelines for Follow-up of Carriers of Hemoglobin Variants Detected by Newborn Screening* (Atlanta: CORN, 1995).
[139] J. E. Bowman, "Genetics and African Americans," *Seton Hall Law Review* 27 (1997): 919, 934.
[140] See E. R. B. McCabe and L. L. McCabe, "State-of-the-Art Technology in Newborn Screening," *Acta Pediatrics* 432 suppl. (1999): 58.
[141] See, e.g., B. Wilfond and N. Frost, "The Cystic Fibrosis Gene: Medical and Social Implications for Heterozygote Detection," *Journal of the American Medical Association* 263 (1990): 2777.
[142] Natowicz and Alper, "Triumphs, Problems, and Controversies," 479.
[143] American Association of Pediatrics, "Newborn Screening Fact Sheets," 454.
[144] Based on data that established this benefit, a national panel recommended universal newborn screening for sickle cell disease. National Institutes of Health Consensus Conference, "Newborn Screening for Sickle Cell Disease," 1205.
[145] Carriers for autosomal recessive genes are themselves healthy. For these disorders to manifest, an individual must inherit two mutant gene copies, one from each parent. See Chapter 1, page 16.

testing to help them make future reproductive decisions.[146] The value of this benefit, however, is uncertain.[147] For example, one research study for cystic fibrosis screening showed that for most families, receipt of a positive newborn test result did not influence future reproductive decisions.[148]

### *Psychosocial Benefits*

Some commentators suggest that even in the absence of a useful medical intervention, newborn screening for early diagnosis of genetic disorders that manifest later in childhood can provide psychosocial benefits. These commentators state that early diagnoses may relieve parental anxieties associated with initial and sometimes confusing onset of symptoms, prepare parents to make practical decisions about life with a disabled child, and allow parents to take advantage of newly developed interventions.[149] In some programs, this putative benefit, along with the benefit of alerting parents to their future reproductive risks, provided the rationale for newborn screening for Duchenne muscular dystrophy,[150] a muscular degenerative condition, and cystic fibrosis.[151]

### *Cost-Benefit for Society*

States generally consider the societal costs and benefits of a particular screening test as one factor in decisions about whether the test should be performed. Some commentators point to societal cost savings as a primary factor in the drive for PKU screening.[152] A cost-

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[146] See page 157, this chapter. If both parents are carriers, subsequent pregnancies carry a one in four risk for the disorder.

[147] See, e.g., Chapter 5, page 115.

[148] E. H. Mischler et al., "Cystic Fibrosis Newborn Screening: Impact on Reproductive Behavior and Implications for Genetic Counseling," *Pediatrics* 102 (1998): 44, 46–47. In thirty-one families in which cystic fibrosis was diagnosed in the first child, forty-three subsequent pregnancies were reported. Prenatal diagnosis was used in nine pregnancies and three fetuses were determined to have cystic fibrosis; all were carried to term. Only five couples reported decisions to have no future children based on cystic fibrosis diagnosis of their first child. Other studies, however, have shown different results. See Chapter 5, page 119.

[149] American Academy of Pediatrics, "Newborn Screening Fact Sheets," 452–454; P. D. Phelan, "Neonatal Screening for Cystic Fibrosis," *Thorax* 50 (1995): 705; see also Clayton, "Screening and Treatment of Newborns," 102–103.

[150] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 261; A. Drousiotou et al., "Neonatal Screening for Duchenne Muscular Dystrophy: A Novel Semiquantitative Application of the Bioluminescence Test for Creatine Kinase in a Pilot National Program in Cyprus," *Genetic Testing* 2 (1998): 55, 56.

[151] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 66. Some states began screening for cystic fibrosis as early as 1982, in the absence of any clear benefit to the newborn. More recent research may provide evidence that early nutritional intervention may benefit newborns diagnosed with cystic fibrosis. See also page 143, this chapter.

[152] Clayton, "Screening and Treatment of Newborns," 128–130; Holtzman, "What Drives Newborn Screening?" 804.

benefit analysis compares the monetary and nonmonetary costs of early disease detection and intervention with the costs incurred by late diagnosis.[153] PKU screening provides an example of how newborn screening can save costs for society. The cost of screening is much less than the costs of treating and supporting affected patients, many of whom previously required long-term institutionalization.[154] Cost-benefit analysis, however, ignores the distribution of costs (e.g., whether dietary supplement costs are supported by families, insurers, or the state) and does not consider indirect and intangible harms.[155]

### Risks of Newborn Screening

#### *Limited Test Validity*

The clinical validity of some newborn screening tests, that is, the positive and negative predictive value of a test result, has not been established by clinical trials.[156] Some commentators argue that while many tests appear to provide benefits, formal confirmation of validity by pilot testing is critical, especially when parents are not given an opportunity to object to screening.[157] One commentator has noted that political factors and zeal, combined with incomplete technical understanding and limited experimental data, can obscure critical thinking in this area.[158] The history of the early implementation of newborn PKU screening provides a cautionary model — some affected children were not detected, and other children were falsely identified as PKU positive.[159] Even for validated tests, inadequate test performance in the testing laboratory may generate incorrect test results.[160] In cases where affected children are not detected by newborn screening, the very existence of screening programs may decrease physician vigilance for clinically symptomatic patients.[161]

#### *Limited Test Utility*

The IOM Committee recommended that state newborn screening should be limited to disorders for which beneficial treatment is available.[162] More recently, the NIH-DOE Task Force on Genetic Testing stated that newborn testing without parental

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[153] For discussion on uses and limits of cost-benefit analysis in policy decisions for genetic testing, see Clayton, "Screening and Treatment of Newborns," 128–129; see also New England Regional Genetics Group, "Optimizing Genetics Services," 60–61.

[154] Natowicz and Alper, "Triumphs, Problems, and Controversies," 479.

[155] Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 148. Intangible and indirect costs include costs associated with false positive results and risks associated with maternal PKU. See page 163, this chapter.

[156] Holtzman, "Genetic Screening and Public Health," 1275. For a definition of clinical validity, see Chapter 2, page 41.

[157] President's Commission, *Screening and Counseling for Genetic Conditions*, 8; Brown, "Metabolic Screening," 1998.

[158] N. Fost, "Ethical Implications," 2814.

[159] See page 142, this chapter.

[160] Clayton, "Screening and Treatment of Newborns," 104; American Academy of Pediatrics, "Issues in Newborn Screening," 347.

[161] See, e.g., American Academy of Pediatrics, "Newborn Screening Fact Sheets," 455.

[162] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 100.

consent should be performed only if safe and effective clinical interventions are available to infants who test positive.[163] Some states, however, have implemented tests in the absence of clinical interventions. For example, newborn screening for sickle cell disease was performed by many states in the 1970s, before the efficacy of prophylactic antibiotic therapy was established.[164] Some states implemented screening for cystic fibrosis, often not diagnosed until several years after birth, in the absence of established medical interventions.[165] More recent data suggest that genetic screening diagnosis of cystic fibrosis at birth and implementation of nutritional therapy may significantly improve long-term health,[166] but some remain unconvinced and cite potential health risks that may be indirectly associated with treatment.[167] For other disorders, mandated testing was withdrawn when data showed that the conditions did not require treatment.[168]

Others also have commented on the inappropriateness of newborn screening for conditions for which interventions are only partially effective.[169] For example, some claim that newborn screening for branched chain ketonuria (also called maple syrup urine disease because of the smell of the urine of affected children) allows intervention only at a point when significant physiological damage has already occurred; diagnosis by newborn screening prevents death, but not lifelong disability.[170] The IOM Committee stated that such interventions of equivocal benefit may present parents with "quandaries

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[163] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing,* 12.

[164] In some population-based sickle cell screening programs in the 1970s, testing resulted in significant harms to some individuals identified as carriers. For a discussion, see Chapter 5, page 114. R. Murray, "The Ethics of Predictive Genetic Screening: Are the Benefits Worth the Risk?" in *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp (Tuskegee, AL: Tuskegee University, 1997), 139; D. Wertz, "Sickle Cell Testing: Past and Present," *The Gene Letter* (July 1996), website: *http:// www.geneletter.org*, visited January 29, 1998.

[165] Holtzman, "Genetic Screening and Public Health," 1275; Holtzman, "What Drives Neonatal Screening Programs?" 802, 803.

[166] P. M. Farrell et al., "Nutritional Benefits of Neonatal Screening for Cystic Fibrosis," *New England Journal of Medicine* 337 (1997): 963; J. E. Dankert-Roelse and G. J. TeMeerman, "Screening for Cystic Fibrosis: Time to Change Our Position?" *New England Journal of Medicine* 337 (1997): 997.

[167] Dr. Norman Fost, Department of Pediatrics, University of Wisconsin, presentation to the New York State Task Force on Life and the Law, January 14, 1998. See also Centers for Disease Control and Prevention, "Newborn Screening for Cystic Fibrosis: a Paradigm for Public Health Genetics Policy Development — Proceedings of a 1997 Workshop," *Morbidity and Mortality Weekly Report* 46 (1997): 1, 9.

[168] Holtzman, "Genetic Screening and Public Health," 1275. Examples include testing for histidinemia and neonatal tyrosinemia.

[169] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 263; Holtzman, "Genetic Screening and Public Health," 1276.

[170] Holtzman, "Genetic Screening and Public Health," 1276.

about whether to treat or not to treat."[171] Another committee stated that in such cases, "families may prefer not to receive the information."[172]

### *Disruption of Family Relationships*

#### *Parental Anxiety and Misperceptions*

One potential risk of newborn screening is the generation of parental anxiety. Many preliminary screening tests are designed to screen a population quickly and inexpensively and may generate false positives that require more accurate follow-up.[173] Notification of the primary screening test result may cause considerable anxiety to parents of a healthy child and may interfere with the developing parent-child relationship. Studies of the effect of false positive diagnoses for congenital hypothyroidism[174] and cystic fibrosis[175] showed significant and long-lasting effects on parental perceptions. Because of these potentially adverse effects, the IOM Committee stated that "accurate and timely confirmatory tests" are essential to newborn screening programs.[176]

Hemoglobinopathy testing incidentally discloses newborn carrier status.[177] Carrier status generally has no affect on a child's health, but parental notification may result in misperceptions, even after extensive counseling.[178] This can cause anxiety, overprotectiveness, destabilization of tenuous parental relationships, or social stigmatization.[179]

#### *Misattributed Paternity*

An additional risk arises when parents of a child identified to have a disorder or carrier status seek follow-up reproductive carrier testing. Parental testing may inadvertently reveal that the putative father of the child is not the biological father.[180]

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[171] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 263. As of 1997, twenty-two states (including New York) screened for the disorder. Hiller, Landenburger, and Natowicz, "Public Participation in Medical Policy Making," 1282.

[172] President's Commission, *Screening and Counseling for Genetic Conditions*,

[173] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 66, 262–263; Kwon and Farrell, "False-Positive Newborn Screening Test Results," 714. Kwon and Farrell estimate that for some disorders commonly screened for by newborn screening programs, there may be more than fifty false positive screen test results for every true positive result.

[174] See Clayton, "Screening and Treatment of Newborns," 119.

[175] A. Tluczec et al., "Parent's Knowledge of Neonatal Screening and Response to False Positive Cystic Fibrosis Testing," *Journal of Developmental and Behavioral Pediatrics* 13 (1992): 181; see also Mischler et al., "Cystic Fibrosis Newborn Screening," 50.

[176] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 66.

[177] See page 157, this chapter.

[178] Dr. Norman Fost, Department of Pediatrics, University of Wisconsin, presentation to the New York State Task Force on Life and the Law, January 14, 1998; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 262.

[179] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 262; also Clayton, "Screening and Treatment of Newborns," 103.

[180] See Chapter 3, page 73; Chapter 4, page 100.

This risk is generally under-appreciated, but anecdotal accounts demonstrate its potentially disastrous effects.[181] The identification of mispaternity in this context, unlike in the context of screening parents for tissue or organ donation, cannot easily be withheld from parents because the findings are central to the future decision making for which the testing is performed. Considering the benefits and risks, a 1983 presidential commission on genetic screening and counseling recommended that misattributed paternity should be disclosed with appropriate counseling.[182] By contrast, the IOM Committee recommended that information about misattributed paternity should not be volunteered to the putative father.[183]

### *Risks to Future Children of Individuals Identified by Newborn Screening*

As a result of newborn screening for PKU in the United States, there are now approximately 3,000 women of reproductive age who have PKU.[184] Children of PKU-positive women are not at significant risk for PKU because of the low chance that a woman's partner will be a PKU carrier.[185] However, these children are at high risk for mental retardation and other congenital defects if their mothers do not strictly adhere to PKU dietary restrictions during pregnancy.[186]

For women with PKU, one commentator described the dietary efforts required to maintain a safe pregnancy as "awesome."[187] A study begun in 1984 to assess over 400 pregnancy outcomes for women with PKU found few well-controlled pregnancies, leading some commentators to remark that all the social benefits of screening may be

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[181] E. T. Juengst, "Caught in the Middle Again: Ethical Considerations in Genetic Testing for Health Risks," *Genetic Testing* 1 (1998): 189, 194.

[182] President's Commission, *Screening and Counseling*, 59–62; the Commission noted that in some situations, circumstances may preclude full disclosure.

[183] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 6, 163.

[184] American College of Obstetricians and Gynecologists News Release, "ACOG Advises a Restricted Preconception Diet for Women with PKU," American College of Obstetricians and Gynecologists website: *http://www.acog.org/from_home/publications/press_releases/nr12-31-99.htm*, visited January 4, 2000.

[185] The chance that a child with a PKU mother will inherit a PKU allele from both parents is 1 in 120. American College of Obstetricians and Gynecologists Committee on Genetics, *Maternal Phenylketonuria*, "Committee Opinion 230 (Washington, D.C.: January, 2000). See also Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 137, 146.

[186] Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 137, 146. Children born to mothers with PKU who do not maintain strict dietary control during pregnancy are at over 90 percent risk of retardation and 12 to 15 percent risk for other congenital birth defects, resulting from exposure to high maternal blood phenylalanine levels during pregnancy. See also S. E. Waisbren et al., "Outcome at Age Four Years in Offspring of Women with Maternal Phenylketonuria: The Maternal PKU Collaborative Study," *Journal of the American Medical Association* 283 (2000): 756.

[187] C. R. Scriver, "The Hyperphenylanemias of Man and Mouse," *Annual Review of Genetics* 28 (1994): 144.

neutralized by adverse birth outcomes in the next generation.[188] The AAP Committee on Genetics recommends that "maintaining contact with women of childbearing age affected with PKU is extremely important."[189] A committee opinion of the American College of Obstetricians and Gynecologists (ACOG) also emphasizes the importance of preconception counseling and pregnancy management of PKU women by specialty centers and care providers.[190]

### *Risks Associated with Research Use of Newborn Blood Samples*

Some state public health agencies use residual newborn bloodspots for epidemiologic research, such as research to determine the prevalence of particular disease-associated gene mutations in regional and ethnic populations.[191] If sample identifiers are retained, there is a potential risk of discrimination against the research subjects because of possible disclosure of genetic information about individuals to third parties.[192] Some also have argued that use of anonymized samples for genetic research still poses harms to individuals in certain ethnic or racial groups that may be subject to stigma as a result of misuse of research results.[193]

## New Technologies and Tests: Opportunities and Challenges

The Human Genome Project presents both opportunities and challenges to state newborn screening programs. The decades-old warning of the NRC that states must exercise caution and restraint in the composition of newborn screening panels while faced with "the increasing number of conditions for which screening will become available" is relevant again.[194] Several policy groups and other commentators have affirmed the value of state newborn screening programs but have called on programs to address certain key issues to ensure fair, safe, and efficacious testing.[195]

Emerging testing technologies, such as DNA chip technology and TMS, may present both opportunities and challenges to state program infrastructure and administration. For example, the high instrumentation and operation costs of TMS may

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[188] Paul, "The History of Newborn Phenylketonuria Screening in the U.S.," 146.
[189] American Academy of Pediatrics, "Issues in Newborn Screening," 348.
[190] American College of Obstetricians and Gynecologists Committee on Genetics, *Maternal Phenylketonuria*.
[191] See page 155, this chapter.
[192] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 6; see also Chapter 7, page 194.
[193] See Chapter 7, page 196.
[194] See page 143, this chapter.
[195] President's Commission, "Screening and Counseling for Genetic Conditions"; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*; NIH-DOE Task Force for Genetic Testing, *Promoting Safe and Effective Genetic Testing*; Holtzman, "Genetic Screening and Public Health"; Hiller, Landenberger, and Natowicz, "Public Participation in Medical Policy Making"; Clayton, "Screening and Treatment of Newborns"; Stoddard and Farrell, "State-to-State Variations in Newborn Screening Policies"; Brown, "Metabolic Screening," 384; Levy, "Tandem Mass Spectrometry: A New Era," 2402.

make it too expensive for some programs.[196] Since the adoption of TMS-based screening tests by a few states, press reports have highlighted state-by-state disparities and the potential effect on identifiable newborns who have either received or been denied the benefits of screening.[197] This has prompted some to question why certain screening tests are performed in other states but not their own. A potential solution would be for state health departments to form partnerships among themselves or with academic or commercial testing laboratories.[198] For example, one commercial genetic testing laboratory that has pioneered the use of TMS for automated, high-volume newborn screening for "more than thirty clinically significant and manageable diseases that affect newborns" contracts testing from some states and other countries.[199]

A key challenge will be to establish criteria and develop processes by which tests are added (and deleted) from a state's newborn screening panel. Some commentators opine that programs must move from the traditional, extemporaneous model to an evidentiary model that uses formal criteria and processes.[200] There is general agreement on some key issues. For example, most agree that testing only should be performed for the immediate and direct benefit of the newborn and that potential reproductive and/or psychosocial benefits to the parents do not in themselves justify newborn screening.[201] Most also advocate universal screening instead of targeted screening of special

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[196] See Levy, "Tandem Mass Spectometry: A New Era," 2402; L. Sweetman, "Newborn Screening by Tandem Mass Spectrometry (MS-MS)," *Clinical Chemistry* 42 (1996): 345, 346. Sweetman notes, however, that the cost of equipment is decreasing as new instruments are developed.

[197] S. Brink, "Little-Used Newborn Test Can Prevent Real Heartache," *US News and World Report*, website: *http://www.usnews.com/usnews/issue/000117/nycu/babies.htm*, visited January 19, 2000; C. Goldberg, "Screening Newborns Can Defeat Hereditary Diseases," *New York Times*, February 26, 2000, A1; C. Ghosh, "Medical Breakdown," *Forbes*, May 29, 2000, at Forbes website: *http://www.forbes.com/forbes/00/0529/6513174a.htm*, visited June 2, 2000.

[198] Levy, "Tandem Mass Spectrometry: A New Era," 2402; Stoddard and Farrell, "State-to-State Variations," 563; American College of Medical Genetics, "ACMG Statement: Tandem Mass Spectrometry in Newborn Screening."

[199] Neo Gen Screening website: *http://www.neogenscreening.com/neogenservices.htm*, visited January 28, 1999. For example, in 1997, the state of North Carolina initiated a pilot study with Neo Gen to determine whether TMS technology should be established in the state laboratory. E. Lengerich et al., "Meeting the Challenges of Genetics and Public Health: State Perspectives on Program Activities — North Carolina," presentation at the First Annual Conference on Genetics and Public Health, Atlanta, May 1998. See also Ghosh, "Medical Breakdown."

[200] Wilfond and Nolan, "Lessons from Cystic Fibrosis," 2950; Holtzman, "What Drives Neonatal Screening Programs?" 804; see also Centers for Disease Control and Prevention, "Newborn Screening for Cystic Fibrosis: a Paradigm," 10; Newborn Screening Task Force, "A Blueprint for the Future," 414.

[201] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 5; New England Regional Genetics Group, "Optimizing Genetic Services," 29; Clayton, "Screening and Treatment of Newborns," 140. The NIH-DOE Task Force on Genetic Testing took a different position, recommending that screening for the purpose of identifying parental reproductive risks was appropriate if the intention is communicated to parents and their written consent is obtained. NIH-DOE Task Force for Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 12.

populations.[202] Established clinical validity of a test is another criterion; a test must be adequately sensitive (detect true positives) and specific (exclude false positives); programs must specify what levels are acceptable.[203] On other issues, however, there is less agreement. For example, should the disorder screened for have a specified degree of severity? Should genetic newborn screening tests be performed only for single-gene disorders, for which clinical predictive value is virtually 100 percent? Who should be making the decisions about state programs, and what authority and resources are available to make recommended changes?

Some groups, including the Newborn Screening Task Force[204] and some state programs, have outlined criteria for screening tests, and a few states have revamped their newborn screening panels. In the early 1990s, Wisconsin altered its legislation for newborn screening, striking the names of specific tests to be included in the newborn panel and replacing them with statutory language that authorizes "blood tests for congenital and metabolic disorders as specified by the department."[205] The Wisconsin Department of Health and Human Services promulgated new regulations and formed a newborn screening advisory group. A subcommittee of the advisory group specified the following formal criteria for inclusion of a test in the newborn screening panel: (1) disease incidence at least 1/100,000, (2) demonstrated reduction in morbidity and mortality, (3) potential for effective therapy, (4) costs comparable to those for established tests such as PKU, and (5) laboratory feasibility. [206] Based on these criteria, Wisconsin deleted testing for branched chain ketonuria and homocysteinuria and added tests for biotidinase deficiency, congenital adrenal hyperplasia, and cystic fibrosis.[207]

More recently, the Commissioner of the Massachusetts Department of Public Health convened an advisory committee to consider testing criteria, review its established mandatory screening panel, and consider new tests and testing technology.[208] The new tests considered were cystic fibrosis testing and testing for twenty additional metabolic disorders that are detectable by TMS. The committee decided that only one metabolic disorder, MCADD (medium chain acyl CoA dehydrogenase deficiency),[209] met the

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[202] National Institutes of Health Consensus Conference, "Newborn Screening for Sickle Cell Disease," 1206.

[203] NIH-DOE Task Force for Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 12; Holtzman, "Genetic Screening and Public Health," 1275.

[204] Newborn Screening Task Force, "A Blueprint for the Future," 394.

[205] Stoddard and P. M. Farrell, "State to State Variations in Newborn Screening Policies," 563.

[206] Ibid.

[207] Two of the tests deleted, branched chain ketonuria and homocysteinuria, are included in New York's screening panel, and two added tests, congenital adrenal hyperplasia and cystic fibrosis, are not.

[208] "Mass. May Increase Infants' Genetic Tests," *American Medical News*, May 18, 1998, 13. Telephone interview with Dr. Anne Marie Comeau, Deputy Director, New England Newborn Screening Program of University of Massachusetts Medical School, October 5, 1999. The new testing technology considered was tandem mass spectrometry.

[209] See "Fact Sheet: MCAD Deficiency," HuGE Net website: *http://www.cdc.gov/genetics/hugenet/factsheets/fmcad.htm*, visited June 20, 2000.

criteria for inclusion in the mandatory screening panel.[210] The committee also recommended the implementation of two pilot screening programs, one for cystic fibrosis testing and the other a multiplex TMS analysis to detect nineteen metabolic disorders.[211] The pilot studies, initiated in February 1999, require IRB approval; they also require that parents be informed about the tests and given the opportunity to refuse.[212]

## Conclusions and Recommendations

### Basic Requirements for Newborn Screening Tests

**New York's Newborn Screening Program panel should be restricted to tests that detect congenital disorders characterized by serious and irreparable harm that can be avoided or minimized only by prompt application of confirmed medical interventions. The analytical and clinical validity of the screening tests also must be confirmed.**

New York's Newborn Screening Program test panel should include only tests that provide an established and direct medical benefit to newborns and for which prompt medical intervention is needed to prevent or minimize symptoms associated with the disorder the test is designed to detect. To justify its use of *parens patriae* power to prevent clear harm to infants, the state's newborn screening program should not include tests that could be performed as effectively in another manner, for example, during standard clinical pediatric care. Newborn screening should not be performed solely for the purpose of preventing future parental anxiety (e.g., testing for a childhood-onset disorder such as Duchenne muscular dystrophy), for the purpose of detecting reproductive carrier status, or for saving societal costs.

Screening tests also must show clear analytical and clinical validity. Tests or combinations of tests used to screen for any given disorder must have acceptable levels of clinical sensitivity (detecting true positives), specificity (minimizing false positives), and clinical predictive value. The Task Force recognizes the possibility that well-intentioned advocates of screening may call for adoption of tests before these criteria are satisfied.

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[210] Telephone interview with Dr. Anne Marie Comeau, October 5, 1999; see also University of Massachusetts Medical School website: *http://www.umassmed.edu/nbs*.

[211] For a discussion of multiplex testing, see Chapter 5, page 128.

[212] A. M. Comeau and R. B. Parad, "Dissent as a Mechanism to Provide Choice in Population-Based Public Health Studies: Implementation and Preliminary Analysis," presentation at the American Society of Human Genetics annual meeting, San Francisco, October 19–23, 1999.

**Statutory Authorization for New York's Newborn Screening Program**

**The New York Public Health Law § 2500-a should be amended to delete the names of individual disorders screened for by the Newborn Screening Program. The law should designate the Commissioner of Health to specify in regulations those congenital disorders for which screening should be performed.**

One commentator has referred to New York's newborn screening list as a "laundry list" of disorders.[213] Since its establishment, New York's screening panel composition has been changed several times, both to add and to remove particular tests. Despite these changes, the current list does not precisely define the screened disorders.[214] To ensure greater precision in the description of disorders screened for, and to retain flexibility in the composition of the screening panel, the law should be amended to remove the specific list of disorders. The law should stipulate that screening tests may be added to the panel at the discretion of the Commissioner of Health. It also should stipulate that all screening tests, including those listed in the newborn screening statute, may be deleted from the panel at the direction of the Commissioner of Health.

**Informing Parents about Newborn Screening**

**The Commissioner of Health should promulgate regulations to require the Newborn Screening Program to provide educational materials about screening to prenatal care providers, as well as to hospitals and institutions of birth. Prenatal care providers should be required to provide and be available to discuss these materials during the course of prenatal visits. Program materials should be multilingual and at appropriate reading levels for a general audience. They should explain the purpose of screening and provide a description of the disorders screened for, their population incidence, and the follow-up process for infants with a positive screen test result.**

Informing parents about newborn screening tests and the screening process shows respect for parents and is likely to foster acceptance of the screening program. Providing parents with information about the testing process, including information about the potential for false positive screening test results, also may reduce parental anxiety associated with cases in which newborns screen positive for a disorder and require additional follow-up.

We agree with the Newborn Screening Task Force that the optimal time to inform and educate parents about newborn screening is during routine prenatal clinical care visits. To enhance chances that parents are informed, and in acknowledgment of the fact

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[213] Clayton, "Screening and Treatment of Newborns," 133.

[214] The law stipulates screening for "homozygous sickle cell disease" rather than for a group of related hemoglobinopathies.

that not all women obtain recommended prenatal care, it also is essential that mothers be informed at the hospital or other institution of birth. New York's Newborn Screening Program should be required to provide prenatal care providers, as well as institutions of birth, with brochures that describe newborn screening and provide a brief description of the disorders screened for. Public health regulations should be amended to clearly establish the responsibilities of newborn screening program personnel, health care providers, and hospitals in the performance of these responsibilities.

Currently, New York's Newborn Screening Program produces brochures in three languages. The program should continue to produce such brochures, updated as appropriate, and in enough languages as is reasonable and reflective of the state population.

### Mandatory Newborn Screening

**New York's Newborn Screening Program should be mandatory for all infants born within the state, provided that several conditions are met: (1) all screening tests must meet the criteria described above in the recommendation concerning the basic requirements for newborn screening tests; (2) parents must be informed and receive educational materials about the program, its goals, and the screening process; and (3) the state must ensure that newborns identified as positive in screening tests are promptly diagnosed and that identified newborns and their families have access to follow-up medical care and counseling related to the disorder, regardless of their ability to pay. New York Public Health Law § 2500-a should be amended to remove the right of parents to assert religious objections to screening.**

The majority of Task Force members agree that newborn screening tests that meet specific criteria should be mandatory. Critical to this decision is the balance of potential benefits and harms of newborn screening. Although the chances of any individual newborn testing positive for a disorder are low, for example, 1 in 12,000 for PKU, several hundred affected infants are detected by New York's program annually.[215] For these children, a parent's decision to forgo screening is tantamount to a refusal of a medical treatment to prevent serious harm, given that the effectiveness of treatment depends on identifying affected newborns before symptoms of the disorder become apparent. The risks of screening, which are primarily associated with the potential for false positive results, are minimal compared to the benefit of avoiding such serious harm. In such circumstances, the autonomy of parents to make health care decisions for their minor children must give way to the state's role, as *parens patriae*, in protecting children from

[215] This figure excludes detected HIV positive newborns. See page 149, this chapter.

harm. As with other medical interventions to prevent serious disease, including other prophylactic measures deemed standard of care for newborns,[216] the fact that a parent's objections may be motivated by religious reasons does not justify placing the child at risk.[217]

Another important factor is the practical difficulty, given the timing of screening and the complex information required to appropriately educate parents, in ensuring that parental consent would be meaningful.

**Follow-up Evaluation and Diagnosis of Screen-Positive Newborns**

**The Newborn Screening Program should ensure that follow-up testing and diagnostic evaluation of newborns who test positive on a screening test is rapid and readily accessible, to maximize treatment benefits for affected newborns and to minimize potential anxiety associated with an initial false positive test result.**

New York's Newborn Screening Program has established processes and systems to promote rapid follow-up testing and diagnosis of newborns who test positive on the initial screening test. For example, prior to notifying physicians of a positive result for an initial screening test, the program performs confirmatory testing of the original bloodspot with a more specific second test to eliminate many false positives, thereby reducing the number of parents who are informed of a positive screening test result. The program also has established an automated telephone system to enable prompt and easy follow-up of screen test results by a newborn's responsible physician. It is still possible, however, for infants to fall through the cracks and become lost to follow-up because of birth outside a hospital or failure on the part of a physician or parent to ensure follow-up of presumptive positive newborns. The program, aided by the newborn advisory committee[218] and the

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[216] See, e.g., page 151, this chapter, discussing two New York State-mandated prophylactic treatment measures for newborns, vitamin K injection and eye prophylaxis.

[217] The Supreme Court has made clear that parents do not have the right to risk grave injury to a child's health even when motivated to do so for religious reasons. See *Jehovah's Witnesses v. King County Hospital*, 390 U.S. 598, 88 S. Ct. 1260 (1968) (per curiam) (authorizing states to override a parent's refusal of a blood transfusion for a minor child). Accord *Matter of Sampson v. Taylor*, 29 N.Y.2d 900, 328 N.Y.S.2d 686 (1972) (even though a child's medical condition did not threaten his life or physical health and was not contagious, the court ordered surgery and necessary blood transfusions over his parents' religious objections when the child was going to suffer serious and irreparable developmental and psychological problems without the surgery). State intervention to provide a child, over parental objections, with medical treatment necessary to avoid serious harm to the child, is consistent with the Court's admonition that "parents may be free to make martyrs of themselves," but that "it does not follow that they are free, in identical circumstances, to make martyrs of their children." *Prince v. Massachusetts*, 321 U.S. 158, 170, 64 S. Ct. 438, 444 (1944) (upholding child labor law as applied to guardian who permitted distribution of religious literature by nine-year-old child). We are mindful of the difference between a parental refusal of newborn screening tests and a parental refusal of medical treatments necessary for a child already identified to be at risk. The fact remains, however, that for children who are affected with the relevant disorder, a refusal of testing is tantamount to a refusal of medical care to prevent serious harm and possibly death. See also Chapter 8, page 220.

[218] See recommendation, page 171, this chapter.

establishment of stable funding,[219] should identify these "cracks" and seal them. One approach, considered by the program but not undertaken because of insufficient financing, is to link the screening program database with the department's vital records database, which records all births in the state.

### Follow-up Medical Care for Newborns of Confirmed Positive Newborns

**New York State should ensure that newborns detected to have a congenital condition by newborn screening receive necessary long-term medical and preventive care, into and through adulthood, regardless of ability to pay. The Newborn Screening Program should facilitate efforts to ensure that affected newborns identified by the program obtain necessary and appropriate medical care. The program should assist treatment centers in locating and treating children who are lost to follow-up.**

When states invoke their *parens patriae* power to mandate screening of all newborns, they incur an ethical obligation to ensure follow-up and medical management of newborns identified to be at risk of harm. The Newborn Screening Program and other programs within the New York State Department of Health should ensure that specialty treatment centers and providers are accessible to all children with disorders identified by newborn screening, including those enrolled in managed care programs. We applaud the department's role in efforts to produce treatment care guidelines for sickle cell disease. The screening program should continue to identify obstacles to follow-up care and promote efforts to overcome such obstacles. The state also should aid children and families in obtaining needed financial coverage for medical care through Medicaid and Child Health Plus and other programs and ensure that medical services for the conditions tested for by newborn screening are covered in these programs.

The Newborn Screening Program and the New York State Department of Health also should aid health care providers and programs who seek to find children who have tested positive for a disorder but who become lost to follow-up. Reasons for such losses are complex and can best be addressed by providers at the "medical home" who are knowledgeable about the patient's family and social circumstances. The New York State Department of Health should help these providers obtain the necessary resources and support, including the support of appropriate social service agencies, to ensure continuous medical care of these children.

[219] See recommendation, page 174, this chapter.

Because medical prevention and management of disorders identified by newborn screening is often a lifetime effort, the New York State Department of Health should ensure adequate access to disease prevention and care into adulthood, including services for PKU-positive women who require close monitoring throughout pregnancy to prevent maternal PKU syndrome. New York should follow the lead of other states in establishing a database to track female adolescents and adults with PKU to promote continuous and coordinated counseling and treatment services. These services are expensive, and women needing them are often not eligible for Child Health Plus or other programs available to children and teenagers. New York State should act to ensure coverage of these services for these adults.

**Establishment of a Newborn Screening Advisory Committee**

**New York's public health regulations should establish a newborn screening advisory committee to act in an advisory capacity to the Commissioner of Health and the Newborn Screening Program. The committee should include outside professional and community representatives and should be independent from the screening program. It should meet at least annually to consider new screening tests, solicit community input, and evaluate program infrastructure, policies, and outcomes.**

The Task Force agrees with CORN that the participation of individuals outside of the departmental screening program enhances the credibility and effectiveness of the program. An appropriately constituted newborn screening program advisory committee can play an important role in ensuring that programs provide optimally designed screening panels and follow-up diagnosis, management, and long-term care of affected newborns identified to have a disorder. The many opportunities and challenges facing newborn screening programs can best be addressed by a group of individuals with different areas of expertise, life experiences, and cultural perspectives. The existence and oversight of a formal committee can ensure that processes and criteria used to consider potential new tests are balanced and less subject to extemporaneous methods and the misguided enthusiasm of one or a few individuals. It also promotes periodic, formal review of program administration.

New York Public Health regulations should be amended to direct the Commissioner of Health to establish a newborn screening advisory committee and to specify committee responsibilities. Activities that might be in the purview of the advisory committee include, but are not limited to, the following: (1) establishment of criteria to guide the review of current and proposed screening tests on a case-by-case basis; (2) review of current and proposed screening tests, as necessary; (3) consideration of the fiscal health of the program; (4) consideration of changes in program infrastructure, testing technologies, or program administration, as necessary; (5) establishment of formal policies for storage and research use of newborn bloodspots; (6) evaluation of program

processes and outcomes, including outcomes of newborns who test positive in the screening program; and (7) solicitation of community input.

The advisory committee requires a full range of expertise in the areas of clinical genetics, pediatric specialty medical care, the laboratory sciences, program evaluation, bioethics, law, and the coordination of medical care for children with special needs. Community representation also is essential and should include one or more parents of children identified to have a disorder screened for by the newborn screening panel. Members of the advisory committee should be selected from throughout New York State and should be representative of the state's population diversity.

**Review and Implementation of Newborn Screening Tests**

**A newborn screening advisory committee, and ad hoc specialty subcommittees established by it, should review all tests currently on or under review for New York's screening panel, as well as potentially valuable new tests, and make recommendations to the Commissioner. For tests for which a confirmed medical benefit has not been sufficiently demonstrated, tests should be viewed as human subject research and should require parental informed consent. These tests should be subject to review by an institutional review board to determine the information that should be provided as part of obtaining parental informed consent. All new screening tests should be subject to periodic follow-up evaluation to determine test accuracy and effectiveness of medical interventions.**

In addition to the fundamental requirements of all newborn screening tests,[220] the program should develop guidelines for other assessment criteria of potential new screening tests on a case-by-case basis. Such factors include the economics of screening, the population prevalence of a disorder and the genotypes that contribute to it, and the degree of effectiveness of a preventive intervention. For example, some commentators disagree about whether the degree of clinical prevention associated with one disorder in New York's screening panel, branched chain ketonuria, is sufficient to justify mandatory screening; posttest medical intervention in this case can prevent death but not serious and permanent impairment.[221] Guidelines can help guide case-by-case consideration of the potential benefits and risks of potential new screening tests. New York's newborn screening advisory committee should review criteria outlined by other groups and adapt criteria based on the needs and infrastructure of New York's program.

[220] See recommendation, page 167, this chapter.
[221] For a discussion, see page 161, this chapter.

It is critical that screening tests that lack sufficiently established test validity and/or medical benefits are introduced by a pilot testing program, with full parental consent. It is important that data from pilot programs undergo objective periodic review and that such programs not be maintained if they fail to demonstrate clear and significant benefits to newborns. In some cases, tests added to New York's newborn screening panel may have adequate demonstration of analytical validity, clinical validity, and clinical utility to justify inclusion on the mandatory test panel without the need for parental consent. A potential example is testing for congenital adrenal hyperplasia, not presently on New York's panel but on the panels of fifteen other states, and for which significant data exist to justify newborn screening to prevent early and life-threatening harm.[222]

Tests currently on or under consideration for New York's newborn screening panel that have not undergone review by formal criteria or by a body independent of program officials should be subject to the same review process.

**Universal Performance of Newborn Screening**

**Newborn screening tests should be performed for all newborns, rather than targeted to specific minority populations perceived to be at higher-than-average risk for a particular disorder.**

New York should continue its current practice of screening all newborns for all disorders on the screening panel, including hemoglobinopathies. Targeting of tests based on ethnic or racial background risks missed diagnoses. To the extent economic issues are relevant, targeted testing itself entails costs that may equal or surpass any potential cost savings based on reducing the number of tests performed.

**Financing of the Newborn Screening Program**

**A permanent, stable funding source is needed to enable the program to consider additional tests, implement new tests as needed, consider changes in testing technologies, improve processes and follow-up evaluation, and support the activities of the advisory committee.**

The state, in its exercise of *parens patriae* power to require screening of all newborns, has a responsibility to ensure an adequate and stable funding source for all newborn screening activities, including follow-up and program evaluation.

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[222] Hiller, Landenburger, and Natowicz, "Public Participation in Medical Policy Making," 1282; B. L. Therrell et al., "Results of Screening 1.9 Million Texas Newborns for 21-Hydroxylase Deficient Congenital Adrenal Hyperplasia," *Pediatrics* 101 (1998): 583; see also E. W. Clayton, "What Should Be the Role of Public Health in Newborn Screening and Prenatal Diagnosis?" *American Journal of Preventive Medicine* 16 (1999): 111, 113.

Several sources interviewed by Task Force staff stated that while New York had long been a leader in newborn screening, it has fallen behind. Program officials agree, noting the inability to provide some tests and services because of the lack of a sufficient and stable funding source. Some tests determined by other state committees and professional groups to be appropriate for newborn screening have not been implemented because of lack of financing. A recent state budgetary allocation for the Newborn Screening Program[223] is a positive step, but it is essential that stability of funding guarantee year-to-year provision of screening, follow-up, and evaluation activities.

### Research Use of Anonymized Newborn Bloodspots

**The Newborn Screening Program, consistent with the recommendations in Chapter 7 concerning research use of samples obtained in the clinical context, should permit the use of anonymized samples for research. The program should inform parents that residual bloodspots may be anonymized and used for quality assurance activities or research. Parents should be informed of the potential research value of the samples and of the impossibility of linking research results to any individual newborn.**

Anonymized newborn bloodspot collections that retain certain demographic markers can provide a powerful research resource. The potential for harm to the newborn sample sources or their families is minimal because of the impossibility of linking research results to an anonymized sample source. The Task Force, however, acknowledges concerns that the research use of samples that retain demographic markers, including markers of race and ethnicity, may result in stigma to certain population groups. Balancing the potential benefits and harms of research use of anonymized bloodspots, the Task Force recommends that the Newborn Screening Program develop policies for the appropriate use of anonymized residual bloodspots. Because the mandatory screening program creates a unique population sample set to which many researchers may desire access and because residual samples are exhaustible, the program, with the aid of the newborn screening advisory committee, should prioritize areas of research, including research to promote the health of children, for which newborn sample use is most appropriate.

As with the research use of other anonymized samples obtained in the clinical context, research use of anonymized newborn blood samples requires IRB review. As discussed in the recommendations in Chapter 7, IRB review should ensure that the samples are or will be truly anonymized.[224] IRB review also should determine whether the proposed

[223] See page 155, this chapter.
[224] See Chapter 7, page 212.

research is of such a sensitive nature that it is inappropriate to use anonymized samples without having obtained the subjects', or in this case the subjects' parents, informed consent.

The Task Force believes that research use of anonymized newborn bloodspots generally should not require parental consent.[225] However, Task Force members agree that out of respect for parents and newborns, and to promote community trust in the newborn screening program, parents should be informed about the potential use of residual newborn bloodspots for anonymized research. Educational materials provided to parents during prenatal care and in the birth hospital should inform parents of this possibility, emphasize the benefits of such research, and assure parents that no risks are posed to their newborns or other family members.

### Research Use of Identified Newborn Bloodspots

**Research use of identified newborn bloodspots should be permitted in accord with recommendations in Chapter 7 concerning the research use of identified samples obtained in the clinical context. In addition, investigators who seek to use identified newborn blood samples for research should demonstrate why unidentified samples or alternate sample sources would not suffice. The use of identified samples should require recontact by the New York State Department of Health and informed consent of parents for each research use. The New York State Department of Health should not release samples that retain identifying data to researchers outside the department except for rare circumstances in which the research is directly relevant to the health of a specific newborn.**

Any research use of identified newborn samples, as for research use of other identified samples obtained in the clinical context,[226] should require the review and approval of an IRB and informed consent, in this case, of parents of newborns.[227] These safeguards are important to prevent potential harms associated with disclosure of research results that may be linked to personal identifying information. The Newborn Screening Program, with the guidance of the newborn screening advisory committee, should establish policies that address the types of research that may be appropriate and the processes by which investigators inside and outside the New York State Department of Health could request such samples. The Task Force agrees with other commentators that those requesting identified newborn samples should demonstrate that the research cannot be performed using anonymized samples or another sample source and that the research is consistent with the goals of the screening program.

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[225] For a discussion about the Task Force's recommendation that informed consent is not required for the research use of anonymized samples obtained in the clinical context, see ibid.

[226] Ibid.

[227] Parents also should be given the option to provide informed consent for coding of the sample for future research use, under the conditions discussed in Chapter 7, page 212.

### Research Use of Coded Newborn Bloodspots

**Research use of coded newborn bloodspots should be permitted in accord with recommendations in Chapter 7 concerning the research use of coded samples obtained in the clinical context. The use of coded samples should require recontact by the New York State Department of Health to obtain the consent of parents for the future research use of the samples.**

Any research use of coded newborn samples, as for research use of coded samples obtained in the clinical context,[228] should require the review and approval of an IRB. The IRB review should ensure that the samples are or will be truly coded and should determine whether the research is of such a sensitive nature that it is inappropriate to use coded samples. The research use of coded newborn samples also should require the recontact of parents to obtain their consent to future research use of the samples.

### Policies for Storage of Newborn Bloodspots

**The Newborn Screening Program should establish a formal policy for the storage of residual identified and anonymized bloodspots. The policy should specify potential uses for stored bloodspots and a maximum period of time for which samples may be maintained with personal identifiers.**

The Newborn Screening Program, with advice from the newborn screening advisory committee, should establish formal policies for the conditions and length of storage of identified and anonymized bloodspots. In establishing these policies, the program should consider its potential need of samples for legal reasons, program quality assurance measures, and research uses. It also should consider potential reasons in favor of discarding samples, including concerns about inappropriate use of identified samples and practical concerns such as storage space. The program should consider the potential appropriate research uses of residual newborn bloodspots within and outside of the New York State Department of Health.

### Notification of Parents of Newborn Carrier Status

**When carrier status for a recessive genetic disease is determined as an incidental finding of a newborn screening test, New York's Newborn Screening Program should report that finding to the authorized**

[228] See Chapter 7, page 214.

**physician. Ideally, parents of carrier newborns should be informed of that result and offered appropriate education, counseling, and testing by appropriately trained and credentialed professionals.**

Currently, hemoglobinopathy screening indicates not only those newborns who have inherited a pair of mutant genes and have sickle cell disease or a related hemoglobinopathy but also healthy newborns who have inherited a single mutant gene. Cystic fibrosis screening, and possibly other future tests, also may inadvertently disclose a newborn's carrier status. These newborns may be at risk of later having a child with a disease, and their parents may be at risk of having an affected child in the future if, in fact, both parents are carriers. Task Force members agree that, ideally, parents should be informed of their newborn's carrier status, provided they receive adequate genetic counseling. New York's Newborn Screening program should continue to inform physicians about a newborn's carrier status and require that contracted genetics service centers provide professional counseling and inform parents about carrier status. Physicians receiving information about carrier status should not disclose this information to parents unless the parents are appropriately counseled.

# 7

# *Informed Consent*

Obtaining a patient's informed consent to medical procedures is both a legal necessity and a basic requirement of medical ethics. Informed consent is defined as an agreement to allow a procedure to go forward after having been advised of relevant facts necessary to make that agreement an intelligent one.[1] Examples of relevant facts include the patient's diagnosis, the nature and purpose of the proposed procedure, and the risks and benefits of, and the alternatives to the procedure.[2] Most commentators maintain that the requirement of informed consent applies to decisions about predictive genetic testing.[3]

## Existing New York Law on Informed Consent

### Section 2805-d of the Public Health Law

Since the early part of the twentieth century, New York courts have recognized that, as a matter of common law, physicians may not perform medical procedures on patients without their consent.[4] However, it was only in the late 1950s and early 1960s that courts in New York and other states ruled that physicians must obtain the patient's *informed* consent to medical procedures.[5] It was also at this time that the medical

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[1] See *Black's Law Dictionary* (St. Paul, MN: West, 1979), 701.

[2] See B. R. Furrow et al., *Health Law*, vol. 1 (St. Paul, MN: West, 1995), 415, 417, 424.

[3] See page 189, this chapter. In this chapter, the term "predictive genetic testing" is meant to include presymptomatic, reproductive, and susceptibility testing. For a discussion of these types of testing, see Chapter 3.

[4] See *Schloendorff v. Soc'y of New York Hosp.*, 211 N.Y. 125, 105 N.E. 92 (1914). The right to refuse medical treatment is protected under both the federal and state constitutions. See *Cruzan v. Dir., Missouri Dept. of Health*, 497 U.S. 261, 278–279, 110 S. Ct. 2841, 2851 (1990) (United States Constitution); *Rivers v. Katz*, 67 N.Y.2d 485, 493, 504 N.Y.S.2d 74, 78 (1986) (New York State Constitution). Some courts have suggested that when government is involved in providing medical care, the due process clause of the United States Constitution requires the government to obtain informed consent to the care. See *White v. Napoleon*, 897 F.2d 103, 113 (3rd Cir. 1990); *Clarkson v. Coughlin*, 898 F. Supp. 1019, 1048–1049 (S.D.N.Y. 1995). See also *Norman-Bloodsaw v. Lawrence Berkely Laboratory*, 135 F.3d 1260, 1268–1270 (9th Cir. 1998) (government defendants violated the due process clause in the Fifth and Fourteenth Amendments, and the Fourth Amendment right against unreasonable searches and seizures, when they performed unconsented-to medical tests on bodyily fluids removed from prospective employees during pre-employment medical examinations); *Heinrich v. Sweet*, 62 F. Supp.2d 282, 313 (D. Ma. 1999) (government medical experiment performed on individuals under false pretenses and without informed consent would violate the individuals' constitutional liberty interest in bodily integrity).

[5] See, e.g., Furrow et al., *Health Law*, 410; R. R. Faden and T. L. Beauchamp, *A History and Theory of Informed Consent* (New York: Oxford University Press, 1986), 86–87; *Darrah v. Kite*, 32 A.D.2d 208, 210–211, 301 N.Y.S.2d 286, 290 (N.Y. App. Div. 1969); *Scott v. Kaye*, 24 A.D.2d 890, 891, 264 N.Y.S.2d

community, in response to the developing case law on informed consent, began to wrestle with this issue.[6]

In 1975, the New York legislature codified the informed consent requirements for physicians, dentists, and podiatrists in Section 2805-d of the Public Health Law.[7] Other health care professionals continue to be subject to the informed consent requirements of the common law.[8]

Section 2805-d requires physicians to disclose to their patients the alternatives to, and the reasonably foreseeable risks and benefits of, proposed treatments or procedures "in a manner permitting the patient to make a knowledgeable evaluation."[9] Section 2805-d does not specify the manner in which physicians must impart this information to their patients. In practice, many health care providers have patients sign informed consent forms that state "that the patient has been fully informed and underst[ands] the risks of the procedure[s]," whether or not a discussion with the patient has actually taken place.[10] The general rule in New York is that signed consent forms provide some evidence, but not necessarily conclusive evidence, that the obligation to obtain informed consent was met.[11]

Section 2805-d provides that patients can sue physicians for failing to obtain informed consent if the patient can prove that a reasonably prudent person in the patient's position would not have undergone the treatment or procedure if the person had been fully informed and that the treatment or procedure was the proximate cause of the injuries

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752, 752 (N.Y. App. Div. 1965); M. E. Silber and M. E. Rabar, "Informed Consent: Evolution and Erosion, Part I," *New York Law Journal*, September 4, 1998, 3. See also *Fiorentino v. Wenger*, 19 N.Y.2d 407, 413, 280 N.Y.S.2d 373, 377 (1967) (finding that surgeon was liable for malpractice because he had not explained "the hazards of the operation, the available alternatives [and] the fact that the procedure was not employed by anyone else in th[e] country").

[6] Faden and Beauchamp, *A History and Theory of Informed Consent*, 86–87.

[7] Silber and Rabar, "Informed Consent," 3.

[8] See *Laskowitz v. CIBA Vision Corp.*, 215 A.D.2d 25, 30–31, 632 N.Y.S.2d 845, 849 (N.Y. App. Div. 1995). Section 2805-d provides physicians, dentists, and podiatrists with certain defenses to lack of informed consent claims that are not available to other health care providers. Ibid., 215 A.D.2d at 30–31, 632 N.Y.S.2d at 848–849.

[9] N.Y. Pub. Health Law § 2805-d(1) (McKinney 1999).

[10] T. A. Moore, "Medical Malpractice: Informed Consent Part II," *New York Law Journal*, October 3, 1995, 3.

[11] Ibid. See *Lowery v. Hise*, 202 A.D.2d 948, 948–949, 609 N.Y.S.2d. 456, 456–457 (N.Y. App. Div. 1994) (even though the plaintiff had signed consent form that stated that she had been fully informed and fully understood the risks of and alternatives to a dental procedure, the plaintiff's assertion that she had neither read nor understood the form was sufficient to permit her informed consent claim to go to trial); *Keane v. Sloan Kettering Inst. for Cancer Research*, 96 A.D.2d 505, 464 N.Y.S.2d 548 (N.Y. App. Div. 1983). See also *Davis v. Caldwell*, 54 N.Y.2d 176, 182–183, 445 N.Y.S.2d 63, 66–67 (1981) (signed consent form was not, in and of itself, conclusive evidence that informed consent was obtained).

of which the plaintiffs complain.[12] For example, in *Davis v. Nassau Ophthalmic Services, P.C.*,[13] a patient underwent an eye operation to correct his nearsightedness and the operation further damaged, rather than corrected, his vision. Because the physician had not properly informed the patient about the operation's possible risks and the jury found that a reasonably prudent person in the patient's position would not have agreed to undergo the operation if the person had been fully informed, the appellate court upheld a damage award against the physician.[14]

Patients may not recover damages for lack of informed consent under Section 2805-d if the risks of which they were not informed were "too commonly known to warrant disclosure;"[15] if they told their physicians that regardless of the risks about which they did not want to be informed;[16] if it was not reasonably possible for the physician to obtain consent;[17] if the treatment, procedure, or surgery was performed in response to a medical emergency;[18] or if the physician determined that full informed consent would "adversely and substantially affect the patient's condition."[19]

Section 2805-d's informed consent requirements apply only to treatments and diagnostic procedures that involve "invasion or disruption of the integrity of the body," such as surgery.[20] This rule has sometimes proven to be an insurmountable hurdle for patients who have sued physicians for violation of section 2805-d's informed consent requirements in the context of reproductive genetic testing.[21] For example, in *Karlsons v. Guerinot*,[22] the plaintiff, who had given birth to a disabled child in the past, was not told by her physician about the availability of amniocentesis during a subsequent pregnancy. She then gave birth to a child with Down syndrome.[23] The plaintiff sued her physician for damages arising from her pain, suffering, and mental anguish, claiming that the physician's failure to counsel her about the availability of amniocenteses led her to continue her pregnancy and to give birth without informed consent.[24] The Appellate

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[12] *Flores v. Flushing Hosp. & Med. Ctr.*, 109 A.D.2d 198, 201–202, 490 N.Y.S.2d 770, 773 (N.Y. App. Div. 1985); N.Y. Pub. Health Law § 2805-d(3) (McKinney 1999).
[13] 232 A.D.2d 358, 648 N.Y.S.2d 454 (N.Y. App. Div. 1996).
[14] Ibid., 232 A.D.2d at 358–361, 648 N.Y.S.2d at 455–456.
[15] N.Y. Pub. Health Law § 2805-d(4)(a).
[16] Ibid., § 2805-d(4)(b).
[17] Ibid., § 2805-d(4)(c).
[18] Ibid., § 2805-d(2)(a).
[19] Ibid., § 2805-d(4)(d). This "therapeutic" exception reflects that, in rare circumstances, disclosing complete information to a patient will make the patient "so ill or emotionally distraught" that the disclosure would substantially and adversely affect the patient's condition. See *Canterbury v. Spence*, 464 F.2d 772, 789, 150 U.S.App.D.C. 263, 280 (D.C. Cir. 1972). In such rare cases, physicians may communicate to their patients less information about the proposed procedure or treatment than would ordinarily be required by the informed consent statute. See *Tibodeau v. Keeley*, 208 A.D.2d 610, 611–612, 617 N.Y.S.2d 183, 184 (N.Y. App. Div. 1994).
[20] N.Y. Pub. Health Law § 2805-d(2) (McKinney 1998).
[21] For a discussion of reproductive genetic testing, see Chapter 3, page 49.
[22] 57 A.D.2d 73, 394 N.Y.S.2d 933 (N.Y. App. Div. 1977).
[23] Ibid., 57 A.D.2d at 75, 394 N.Y.S.2d at 934.
[24] Ibid.

Division upheld the dismissal of the claim, pointing out that any harms to the plaintiff were not caused by a violation of her physical integrity.[25]

Although *Karlsons* involved reproductive genetic testing, the requirement of showing an invasion of bodily integrity may make Section 2805-d's informed consent requirements inapplicable to other types of genetic testing as well. Although it did not involve genetic testing, *Hecht v. Kaplan*[26] is instructive in this regard. In *Hecht*, a physician drew a vial of his patient's blood, with the patient's consent, for cytomegalovirus (CMV) testing. While the needle was still inserted in the patient's arm and without receiving the patient's permission, the physician then drew a second vial of blood. He subsequently tested the second vial of blood for the presence of human T-cell leukemia virus (HTLV), without the patient's consent, and told the patient, several months later, that he had tested positive.[27] The patient then sued the physician under Section 2805-d for drawing and testing the second vial of blood without informed consent.[28] The court dismissed the lawsuit, reasoning that the unauthorized testing of the blood without informed consent did not "constitute an affirmative violation of [the patient's] physical integrity."[29]

In *Hecht*, the patient had consented to the needle stick for purposes of the CMV testing. If the needle stick itself were performed without authorization, it is arguable that the requirement of showing an affirmative physical violation would have been met.[30] Nonetheless, even in a case involving an unauthorized needle stick, individuals might still have difficulty succeeding in lawsuits under section 2805-d for lack of informed consent to predictive genetic testing because, in order to prevail in Section 2805-d lawsuits,

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[25] Ibid., 57 A.D.2d at 81–83, 394 N.Y.S.2d at 938–939. See also *Keselman v. Kingsboro Med. Group*, 156 A.D.2d 334, 335, 548 N.Y.S.2d 287, 288–289 (N.Y. App. Div. 1989) (physician's failure to diagnose a fetal genetic anomaly, resulting in birth of child with a genetic disorder, did not violate the mother's right to informed consent because "the wrong complained of did not arise out of some affirmative violation of the plaintiff mother's physical integrity"). Individuals who do not receive proper genetic counseling from their physicians are not remediless. For the last twenty years the New York Court of Appeals has recognized malpractice lawsuits against physicians for giving improper genetic advice in the reproductive genetic testing context, although the damages that are recoverable are somewhat circumscribed. See, e.g., *Martinez v. Long Island Jewish Hillside Med. Ctr.*, 70 N.Y.2d 697, 518 N.Y.S.2d 955 (1987); *Becker v. Schwartz*, 46 N.Y.2d 401, 413 N.Y.S.2d 895 (1978).

[26] 221 A.D.2d 100, 645 N.Y.S.2d 51 (N.Y. App. Div. 1996).

[27] Ibid., 221 A.D.2d at 102–103, 645 N.Y.S.2d at 52.

[28] Ibid., 221 A.D.2d at 102, 645 N.Y.S.2d at 52.

[29] Ibid., 221 A.D.2d a 104, 645 N.Y.S.2d at 53. See also *Doe v. Dyer-Goode*, 389 Pa. Super 151, 566 A.2d 889 (1989) (unconsented-to HIV test on blood drawn with the consent of the patient is not a violation of the patient's bodily integrity for informed consent purposes).

[30] Cf., e.g., *Karlsons*, 57 A.D.2d at 82, 394 N.Y.S.2d at 939 (injections are affirmative violations of a patient's bodily integrity); *DiRosse v. Wein*, 24 A.D.2d 510, 261 N.Y.S.2d 623 (N.Y. App. Div. 1965) (same); *Sangiuolo v. Leventhal*, 132 Misc.2d 680 (Sup. Ct. New York County 1986) (Section 2805-d requires informed consent for therapeutic injections).

plaintiffs must establish that their injuries were "directly" or "medically" caused by the procedures that violated their physical integrity.[31] However, injuries that individuals may suffer as a result of predictive genetic testing, such as psychological trauma or discrimination,[32] are not the "direct" or "medical" result of the needle sticks to draw blood. Rather, they are the result of the disclosure of the genetic information gleaned from the tests performed on the blood after it has been removed from the individual's body. Accordingly, courts may find that section 2805-d has no bearing in the predictive genetic testing context at all.

**The Civil Rights and Insurance Laws**

Sections 79-l of the New York Civil Rights Law and 2612 of the New York Insurance Law, which were both enacted in 1996, prohibit the performance of predictive genetic tests on an individual's biological samples without the individual's prior written informed consent.[33] The requirement of informed consent generally does not apply to routine medical tests performed for nongenetic purposes[34] or if the subject of the test has exhibited symptoms of the disease that the test was designed to predict.[35] Section 79-l applies to everyone except insurers, and Section 2612 applies to insurers and persons who act on behalf of insurers.

Section 79-l defines informed consent as a signed and dated "written authorization" that contains:

- A general description of the test
- A statement of the purpose of the test
- A statement that the individual may wish to obtain professional genetic counseling prior to signing the informed consent form
- A statement that a positive test result is an indication that the individual may be predisposed to or have the specific disease or condition tested for and may

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[31] *Flores v. Flushing Hosp. & Med. Ctr.*, 109 A.D.2d at 200–201, 490 N.Y.S.2d at 772; *Karlsons v. Guerinot*, 57 A.D.2d at 81–82, 394 N.Y.S.2d at 939.

[32] Under certain circumstances, physicians may have a duty under Section 2805-d to inform their patients of the emotional consequences of proposed treatments. See *Perez v. Park Madison Laboratories, Inc.*, 212 A.D.2d 271, 274–275, 630 N.Y.S.2d 37, 40 (N.Y. App. Div. 1995). See also *Jones v. Howard University, Inc.*, 589 A.2d 419, 422 n.5 (D.C. App. 1991) (dictum) ("If a course of treatment includes a risk that it would cause emotional harm or some kind of mental injury, and such a risk were unrevealed and should materialize, the emotionally-harmed person would have a cause of action based on lack of informed consent, even in the absence of physical injury."). For a discussion of the potential harms of genetic testing, see Chapter 3, page 57.

[33] N.Y. Civ. Rights Law § 79-l(2)(a) (McKinney 1999); N.Y. Ins. Law § 2612(a) (McKinney 1999).

[34] N.Y. Civ. Rights Law § 79-l(1)(a) (McKinney 1999); N.Y. Ins. Law § 2612(i) (McKinney 1999).

[35] N.Y. Civ. Rights Law § 79-l(1)(b) (McKinney 1999); N.Y. Ins. Law § 2612(i) (McKinney 1999).

wish to consider further independent testing, consult their physician, or pursue genetic counseling

- A general description of each specific disease or condition tested for
- The level of certainty that a positive test result for the disease or condition serves as a predictor of such disease or condition
- The name of the person or categories of persons or organizations to whom the test results may be disclosed
- A statement that no tests other than those authorized shall be performed on the biological sample and that the sample will be destroyed at the end of the testing process or not more than sixty days after the sample was taken, unless a longer period of retention is expressly authorized in the consent form
- The signature of the subject of the test or, if the subject lacks the capacity to consent, the signature of the person authorized to consent for that individual[36]

Section 2612 contains virtually identical informed consent requirements,[37] and both Sections 79-l and 2612 prohibit waivers of the statutes' informed consent requirements.[38]

The informed consent provisions of Sections 79-1 do not apply to New York's newborn screening program,[39] New York's program for genetically "fingerprinting" convicted criminals,[40] research on anonymous biological samples where an institutional review board (IRB) has approved the research protocol and has assured "the anonymity of the sources of the samples,"[41] and research (regardless of IRB approval) where the research subjects have provided a general waiver for the use of their samples for research, the researchers remove all of the sample identifiers, and the research results cannot be linked to the subjects.[42] Also exempt from the informed consent provisions of Sections 79-l and 2612 are additional predictive genetic testing on a biological sample "to demonstrate the integrity of the sample tested or to resolve the analysis of a test with a previously indeterminate

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[36] N.Y. Civ. Rights Law § 79-l(2)(b)(1-8) (McKinney 1999).
[37] N.Y. Ins. Law § 2612(b)(1-8) (McKinney 1999). Unlike Section 79-l of the Civil Rights Law, Section 2612 does not mandate that the written authorization state that the individual to be tested may wish to obtain professional genetic counseling before signing the authorization.
[38] N.Y. Civ. Rights Law § 79-l(2)(c) (McKinney 1998); N.Y. Ins. Law § 2612(8)(c) (McKinney 1998).
[39] N.Y. Civ. Rights Law §§ 79-l(4)(b), 79-l(7) (McKinney 1998).
[40] Ibid., § 79-l(4)(b).
[41] Ibid., §§ 79-l(4)(a), 79-l(4)(b), 79-l(4)(c), 79-l(7).
[42] Ibid., §§ 79-l(2)(c), 79-l(9).

result"[43] and predictive genetic testing on deceased individuals if the next of kin provides informed consent for the testing.[44]

Predictive genetic testing also may be performed on biological samples without the subject's informed consent if a court orders the tests.[45] Before a court may issue such an order, it must consider "the privacy interests of the individual subject of the genetic test and of close relatives of such individual, the public interest, and, in the case of the medical or anthropological research, the ethical appropriateness of the research."[46]

Willful violators of Section 79-1's informed consent provisions can be charged with a misdemeanor, imprisoned up to ninety days, and fined up to $5,000.[47] Nonwillful violators can be convicted of a violation and fined up to $1,000.[48] Violators of Section 2612's informed consent provisions can be convicted of a misdemeanor, fined up to $5,000, and are subject to cease and desist orders by the Superintendent of Insurance.[49] Except for certain fines and other sanctions that can be levied by the Superintendent of Insurance, individuals and organizations must be proven guilty beyond a reasonable doubt before they may be convicted of a misdemeanor or violation and fined.[50] Sections 79-1 and 2612 do not explicitly authorize private lawsuits against parties who violate their informed consent provisions, and it is unclear whether courts would infer a right to bring such lawsuits.[51]

## The Process of Informed Consent

### Informed Consent Models

Commentators have described two different models of informed consent, the event model and the process model.[52] The event model of informed consent is the model

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[43] Ibid., § 79-l(8).
[44] Ibid., § 79-l(11). The term next of kin is not defined in the statute.
[45] Ibid., § 79-l(4)(c), (d).
[46] Ibid., § 79-l(4)(d).
[47] Ibid., § 79-l(5)(b).
[48] Ibid., § 79-l(5)(a).
[49] N.Y. Ins. Law §§ 2612(j), 109(a), 2406(a), 2406(d) (McKinney 1998).
[50] See N.Y. Penal Law §§ 10.00(3), 55.10 (McKinney 1999); N.Y. Crim. Proc. Law § 70.20 (McKinney 1999).
[51] Compare *Mark G. v. Sabol*, 93 N.Y.2d 710, 718–722, 695 N.Y.S.2d 730, 733–735 (1999) (refusing to find an implied right of action for violation the Child Welfare Reform Act); *Carrier v. Salvation Army*, 88 N.Y.2d 298, 644 N.Y.S.2d 678 (1996) (find private right of action under New York Social Services Law § 460-d); *Larson v. Albany Med. Ctr.*, 252 A.D.2d 936, 936–938, 676 N.Y.S.2d 293, 294–295 (N.Y. App. Div. 1998) (refusing to infer a private right of action against hospital that allegedly violated N.Y. Civ. Rights Law § 79-i by discriminating against staff who refused to participate in abortions) with *Doe v. Roe*, 190 A.D.2d 463, 470–471, 599 N.Y.S.2d 350, 353–354 (N.Y. App. Div. 1993) (inferring a private right of action against persons who disclose HIV information in violation of Article 27-F of the Public Health Law).
[52] See, e.g., P. S. Appelbaum, C. W. Lidz, and A. Meisel, *Informed Consent: Legal Theory and Clinical Practice* (New York: Oxford University Press, 1987), 151–158; G. Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer: The Process and Content of Informed Consent," *Journal of the American Medical Association* 277 (1997): 1467, 1469; N. Press and C. H. Browner, "Risk, Autonomy, and

generally used in medical practice and research. It treats informed consent as a time-limited isolated event that takes place shortly before performing a procedure.[53] By contrast, in the process model, the provider obtains the patient's consent over time through a dialogue in which the provider and the patient discuss the patient's values, as well as the risks, benefits, and alternatives to the particular procedure.[54] This model of informed consent, which has been described as the ideal, "requires great psychological and pedagogical skills" of health care providers.[55]

### Obstacles to Obtaining Informed Consent

Various obstacles to effective physician-patient communications can interfere with a physician's ability to obtain informed consent. Examples include differences in the cultural and educational backgrounds of physicians and patients,[56] time constraints on physician-patient interactions,[57] the difficulty of understanding probabilistic information,[58] and the difficulty of processing large amounts of medical information at one time, that is, "information overload."[59]

For some physicians, an additional obstacle to obtaining informed consent in the context of predictive genetic testing is the physician's own lack of knowledge about genetics and the meaning of genetic test results.[60] A 1996 study by the Human Genome Project indicated that 46 percent of the physicians surveyed had never taken a course in basic genetics.[61] A 1997 study found that almost one-third of the physicians surveyed,

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Responsibility: Informed Consent for Prenatal Testing," *Hastings Center Report* 25, Special Supplement (1995): S9, S10.

[53] Press and Browner, "Risk, Autonomy, and Responsibility," S10; see Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1469.

[54] See Press and Browner, "Risk Autonomy and Responsibility," S10. See P. Schuck, "Rethinking Informed Consent," *Yale Law Journal* 103 (1994): 899, 903–904.

[55] Press and Browner, "Risk Autonomy and Responsibility," S10.

[56] See, e.g., Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1469; Faden and Beauchamp, *A History and Theory of Informed Consent*, 316–318.

[57] See, e.g., B. A. Bernhardt et al., "Prenatal Genetic Testing: Content of Discussions between Obstetric Providers and Pregnant Women," *Obstetrics and Gynecology* 91 (1998): 648, 653.

[58] See, e.g., Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1468; Faden and Beauchamp, *A History and Theory of Informed Consent*, 319–323; Chapter 4, page 91.

[59] S. Elias and G. J. Annas, "Generic Consent for Genetic Screening," *New England Journal of Medicine* 330 (1994): 1611, 1611; Faden and Beauchamp, *A History and Theory of Informed Consent*, 323–324.

[60] See, e.g., Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1468; American Medical Association Council on Ethical and Judicial Affairs, "Multiplex Genetic Testing," *Hastings Center Report* 28, no. 4 (1998): 15, 17–18; National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing in the United States*, ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of Health, 1997), 63; Chapter 3, page 71; Chapter 4, page 92.

[61] See American Medical Association Council, "Multiplex Genetic Testing," 17.

who included medical geneticists and other specialists, incorrectly interpreted results of genetic tests for colon cancer susceptibility.[62] Other studies have found that a significant percentage of obstetricians/gynecologists and family practitioners do not understand the circumstances in which cystic fibrosis, one of the more common genetic diseases, is transmitted from parents to children.[63] In light of these findings, some commentators contend that few physicians in clinical practice have sufficient knowledge to provide the information necessary for a patient's consent to predictive genetic testing to be informed.[64] This problem will only grow larger as the number of genetic tests increases.

The Institute of Medicine Committee on Assessing Genetic Risks (the IOM Committee) recommended that physicians who offer or refer patients for genetic testing should also offer or refer patients for genetic counseling and education prior to the testing.[65] Concerned that most physicians and genetic counselors do not yet have expertise with genetic susceptibility testing for late-onset disorders, the IOM Committee also recommended that such testing should be performed by genetic specialists as part of research projects.[66] The American Medical Association believes that physicians should provide genetic susceptibility testing for breast and ovarian cancer only if they feel able to provide comprehensive pre- and posttest counseling to their patients.[67] If the physicians do not, they should refer patients to specialized genetics centers.[68]

Despite these recommendations, many physicians are reluctant to refer patients to professionals who have both sufficient genetics knowledge and the time to help patients consider the risks, benefits, and alternatives to genetic testing. In general, fewer nongeneticists than geneticists believe that it is necessary to provide extensive genetic counseling to patients about proposed genetic tests.[69] In addition, a 1997 study found that only 17.6 percent of physicians who had ordered genetic tests to detect predispositions to colon cancer had arranged genetic counseling for their patients beforehand and that only 18.6 percent of all of the patients in the study had received genetic counseling before being tested.[70] Another study found that, notwithstanding the recommendations of the American College of Obstetricians and Gynecologists, obstetric providers often did not

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[62] F. M. Giardiello et al., "The Use and Interpretation of Commercial *APC* Gene Testing for Familial Adenomatous Polyposis," *New England Journal of Medicine* 336 (1997): 823, 824.

[63] L. B. Andrews, "Compromised Consent: Deficiencies in the Consent Process for Genetic Testing," *Journal of the American Women's Medical Association* 52 (1997): 39, 40.

[64] See, e.g., American Medical Association Council, "Multiplex Genetic Testing," 17; Chapter 12, page 362.

[65] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 14.

[66] Ibid., 177.

[67] American Medical Association, House of Delegates Resolution H-55.979 (1998).

[68] Ibid. For a detailed discussion of the roles of different health care providers in providing genetic counseling, see Chapter 12.

[69] G. Geller and N. A. Holtzman, "A Qualitative Assessment of Primary Care Physicians' Perceptions about the Ethical and Social Implications of Offering Genetic Testing," *Qualitative Health Research* 5 (1995): 97 (1995).

[70] Giardiello et al., "Commercial *APC* Gene Testing," 824.

refer their patients during their first prenatal visits to genetic providers when concerns about familial genetic diseases arose.[71]

Even on those occasions when physicians discuss predictive genetic testing with their patients, the discussions are often limited. In one study, obstetric providers spent an average of 2.5 to 6.9 minutes discussing genetic testing with their patients, and their discussions with patients about amniocentesis and chorionic villus sampling were usually limited to "the practical details of testing."[72]

### Impact of the Informed Consent Process on Predictive Genetic Testing Decisions

Studies have found that, without being counseled about the risks, benefits, and alternatives to predictive genetic testing, a majority of individuals indicate that they would like to take predictive genetic tests to determine their risk for genetic diseases.[73] This remains true even when individuals are told that there are no treatments for some of the diseases.[74] However, in one study, women who were "very interested" in undergoing BRCA1 testing became less so after being told about the possibility that adverse results could be used against them in employment and insurance decisions and "that most breast cancer was not associated with a BRCA1 mutation."[75] In addition, physicians at Memorial Sloan Kettering Cancer Center in New York report that only 40 percent of patients who undergo genetic counseling for BRCA1 testing actually take the test.[76] However, some studies have found that genetic counseling and education did not

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[71] Bernhardt et al., "Prenatal Genetic Testing," 653.

[72] Ibid., 651, 653.

[73] See, e.g., Press Release, "Majority of New Yorkers Would Take Genetic Test for Heart Disease and Cancer Poll Finds," Albert Einstein College of Medicine, October 7, 1998, 1 (subjects questioned in telephone interview without counseling); E. S. Tambor, B. K. Rimer, and T. S. Strigo, "Genetic Testing for Breast Cancer Susceptibility: Awareness and Interest among Women in the General Population," *American Journal of Medical Genetics* 68 (1997): 43; R. T. Croyle, J. S. Achilles, and C. Lerman, "Psychologic Aspects of Cancer Genetic Testing: A Research Update for Clinicians," *Cancer* 80 (1997): 569, 570–571; N. A. Holtzman et al., "Education about BRCA1 Testing Decreases Women's Interest in Being Tested," *American Journal of Human Genetics* 59 (Supplement) (1996): A56; G. Geller et al., "Informed Consent and BRCA1 Testing," *Nature Genetics* 11 (1995): 3647, 3647.

[74] Albert Einstein College of Medicine, "A Majority of New Yorkers Would Take Genetic Test," 1.

[75] Holtzman et al., "Education about BRCA1 Testing," A56; Geller et al., "Informed Consent and BRCA1 Testing," 3647.

[76] See G. B. Mann and P. I. Borgen, "Breast Cancer Genes and the Surgeon," *Journal of Surgical Oncology* 67 (1998): 267, 272. Other studies have found that the more treatable a genetic condition, the greater patient uptake for genetic tests that detect those conditions. T. M. Marteau and R. T. Croyle, "Psychological Responses to Genetic Testing," *British Medical Journal* 316 (1998): 693. Thus, it is reasonable to conclude that counseling patients about treatment options affects their decisions about whether to undergo testing.

dissuade high-risk patients who are interested in BRCA1 testing from taking the test[77] or change the genetic testing intentions of women at low to moderate risk who had previously indicated a preference regarding BRCA1 testing.[78]

One commentator emphasizes that genetic counseling is usually not judged by its effect on the testing decisions made by individuals, but by whether it has enabled the individuals to "carefully consider" the consequences of different options.[79]

## Content of Informed Consent to Predictive Genetic Testing

Researchers have found that consent forms for predictive genetic testing differ widely in the information they provide and in the language and presentation of the information.[80] Commentators have proposed that providers discuss the following issues as part of the informed consent process to predictive genetic testing.[81]

### The Purpose of the Test

Providers should explain what the tests are designed to detect and why they are performing the tests.[82] For example, patients undergoing BRCA1 testing should be told that the test detects specific genetic mutations that have been associated with a predisposition to breast cancer and that the test is being performed to determine whether the patient has such mutations.[83]

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[77] See Croyle, Achilles, and Lerman, "Psychologic Aspects of Cancer Genetic Testing," 571–572.

[78] C. Lerman et al., "Controlled Trial of Pretest Education Approaches to Enhance Informed Decision-Making for BRCA1 Gene Testing," *Journal of the National Cancer Institute* 89 (1997): 148, 155–156.

[79] Ibid.

[80] S. J. Durfy, T. E. Buchanan, and W. Burke, "Testing for Inherited Susceptibility to Breast Cancer: A Survey of Informed Consent Forms," *American Journal of Medical Genetics* 75 (1998): 82, 85–87; M. K. Cho, M. Arruda, and N. A. Holtzman, "Educational Material about Genetic Tests: Does It Provide Key Information for Patients and Practitioners?" *American Journal of Medical Genetics*, 73 (1997): 314, 316–318. An informal survey of New York State laboratories conducted by the New York State Task Force on Life and the Law revealed a similar pattern.

[81] This section discusses informed consent to predictive genetic testing in the clinical context. Additional informed consent issues arise when genetic testing is performed in the research context. See, e.g., E. W. Clayton et al., "Informed Consent for Genetic Research on Stored Tissue Samples," *Journal of the American Medical Association* 274 (1995): 1786; 45 C.F.R. § 46.116 (1999) (listing informed consent requirements for federally funded research).

[82] See Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1470; M. K. Cho, M. Arruda, and N. A. Holtzman, "Educational Materials about Genetic Tests," 314, 316; American Society of Clinical Oncology, "Statement of the American Society of Clinical Oncology: Genetic Testing for Cancer Susceptibility," *Journal of Clinical Oncology* 14 (1996): 1730, 1732; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 156.

[83] See Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1470; American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732.

## A Description of the Testing Process

Health care providers should describe the testing procedure to their patients.[84] For example, if the testing procedure involves the drawing of blood, the provider should tell the patient about the needle puncture, the amount of blood to be drawn, and that the blood will be sent to a laboratory for testing.[85] The patients also should be given a timetable for learning the test results.[86]

## The Accuracy of Genetic Tests and the Meaning of Their Results

Providers should explain that predictive genetic tests are not always accurate and inform patients about the rates of false positive and false negative results.[87] Commentators also suggest that providers should inform patients about the meaning of positive and negative test results; the test's ability, or lack thereof, to predict a disease's severity; the possible range of severity; and "the possibility that no additional risk information will be obtained at the completion of the test."[88] Some commentators suggest that patients should be told that genetic tests cannot predict with certainty whether a disease will manifest or its age of onset.[89]

### Risks and Benefits of Genetic Testing

As with other medical procedures, informing patients about the risks and benefits of predictive genetic testing is a crucial part of obtaining informed consent. Unlike most medical procedures, however, many of the risks associated with genetic testing do not result from the procedure itself, that is, the needle stick and the drawing of blood. Rather, the risks arise from the information that might be revealed by the test results.[90] These risks include the possibility that the information will be used against the patient in employment or insurance decisions or that it will lead to psychological distress or family conflicts.[91] Benefits of predictive genetic testing may include the ability to better manage

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[84] Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1470; Institute of Medicine Committee on Assessing Genetic Risks , *Assessing Genetic Risks*, 156.
[85] Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1470.
[86] Ibid.
[87] See American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732.
[88] Ibid.; Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1470–1471.
[89] See S. J. Durfy, T. E. Buchanan, and W. Burke, "Testing for Inherited Susceptibility to Breast Cancer: A Survey of Informed Consent Forms for BRCA1 and BRCA2 Mutation Testing," *American Journal of Medical Genetics* 75 (1998): 82, 83.
[90] See National Bioethics Advisory Commission, *Research Involving Human Biological Materials: Ethical Issues and Policy Guidance*, vol. 1 (Rockville, MD: National Bioethics Advisory Commission, 1999), 55. For a discussion of the risks and benefits of predictive genetic testing, see Chapter 3, page 68.
[91] See, e.g., Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1470–1472; American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732.

one's health — for example, by taking advantage of preventive treatments — and "relief from uncertainty."[92]

### Voluntariness of Testing

Commentators recommend that patients should be told that undergoing predictive genetic testing is completely voluntary and that the patient's care will not be adversely affected regardless of whether consent is provided.[93]

### Options for Risk Estimation Other Than Predictive Genetic Testing

Informed consent to a proposed clinical procedure requires a discussion about alternatives to the procedure.[94] In the context of predictive genetic testing for late-onset disorders, where the purpose of the testing is to estimate the risk of future illness, commentators recommend that patients be told about "options for risk estimation other han genetic testing."[95] For example, the American Society of Clinical Oncology has suggested that patients who wish to undergo BRCA1 or BRCA2 testing should be told that breast cancer risk also can be estimated using empiric risk tables for breast cancer based on family history.[96]

## Confidentiality Issues

Genetic test results are private, sensitive information,[97] and their improper disclosure may lead to adverse employment or insurance decisions or other adverse psychosocial consequences.[98] Commentators therefore recommend that a discussion of confidentiality issues should be part of the informed consent process to predictive genetic testing.[99] Such issues include measures to protect the confidentiality of test results, patient and third-party access to test results, and the possibility of breaches of confidentiality by persons to whom the patients release the results.[100]

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[92] Durphy, Buchan, and Burke, "Testing for Inherited Susceptibility," 84.
[93] Cho, Arruda, and Holtzman, "Educational Materials about Genetic Tests," 316; NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 12; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 156.
[94] See page 179, this chapter; Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1472.
[95] American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732.
[96] Ibid. See Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1472.
[97] See, e.g., Durphy, Buchanan, and Burke, "Testing for Inherited Susceptibility to Breast Cancer," 84.
[98] See Chapter 4, page 95.
[99] See Cho, Arruda, and Holtzman, "Educational Materials about Genetic Tests," 316; American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732.
[100] American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732.

### Available Medical Surveillance and Treatment Options, and Their Effectiveness, following Testing

Commentators maintain that prior to providing consent for predictive genetic testing, patients should be told about the treatment and surveillance options, and their effectiveness, that will be available after testing.[101] For example, individuals being tested for Huntington disease should be told that there are currently no treatments for the disease. Individuals undergoing BRCA1 testing should be told that available interventions following testing include increased monitoring; prophylactic surgery that can reduce, but not eliminate, breast or ovarian cancer risk; and prophylactic hormonal therapy whose efficacy is not clearly established and which poses health risks of its own.[102]

### Costs of Testing and Counseling

Commentators recommend that, as part of the informed consent process, individuals who wish to undergo predictive genetic testing should be told the cost of the tests.[103] The American Society of Clinical Oncology also recommends that the individuals be told the costs of pre- and posttest counseling and follow-up care.[104]

## Informed Consent to Multiplex Genetic Testing

Multiplex genetic testing is predictive genetic testing for more than one condition in a single testing session.[105] For example, a recent pilot program offered multiplex prenatal carrier testing for Ashkenazi Jewish couples for gene mutations linked to Tay Sachs disease, Gaucher disease, and cystic fibrosis. [106] Currently, no multiplex testing is offered for late-onset disorders, but commentators predict that such testing will take place in the future.[107]

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[101] Ibid.; Cho, Arruda, and Holtzman, "Educational Materials about Genetic Tests," 316; Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1472.

[102] See Chapter 3, page 65.

[103] American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732; Geller et al., "Genetic Testing for Susceptibility to Adult Onset Cancer," 1472.

[104] American Society of Clinical Oncology, "Genetic Testing for Cancer Susceptibility," 1732.

[105] American Medical Association Council, "Multiplex Genetic Testing," 15. For further discussion of multiplex testing, see Chapter 5, page 128.

[106] C. M. Eng et al., "Prenatal Genetic Carrier Testing Using Triple Disease Screening," *Journal of the American Medical Association* 278 (1997): 1268. See Chapter 5, page 128.

[107] See American Medical Association Council, "Multiplex Genetic Testing," 19–21; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 102, 170; Chapter 5, 130.

While some commentators maintain that providers should obtain full informed consent from patients for each test in a multiplex testing panel,[108] others suggest that informing individuals about detailed aspects of multiple tests may cause "information overload." These commentators instead propose that providers should obtain one "generic consent" to all of the tests in a multiplex panel.[109] The generic consent process would highlight broad concepts and common-denominator issues for all the tests.[110] For example, rather than being told details about each condition tested for, patients who seek to undergo multiple reproductive carrier tests at one time would be told that the tests will reveal whether they have an increased risk of having offspring born with certain physical or mental disabilities.[111] The IOM Committee emphasized that "tests should be grouped into categories of tests and disorders that raise similar issues and implications, both for informed consent and for genetic education and counseling."[112] For example, tests for untreatable disorders should not be grouped with tests for treatable disorders.[113]

Even supporters of the generic consent process do not believe that it should be used in all circumstances. For example, some maintain that generic consent is inappropriate if a multiplex panel includes tests for conditions for which an individual at higher-than-normal risk.[114] The IOM Committee contended that health care providers should use generic consent only when it is not possible for them to supply information about each of the tests individually.[115]

## Informed Consent to Pleiotropic Genetic Testing

A single gene mutation can have multiple unrelated effects and can indicate risks for seemingly unrelated conditions.[116] For example, a particular population variant of a gene called apolipoprotein E (APOE) may aid in determining the proper treatment for coronary artery disease and also has been associated with a risk for late-onset Alzheimer disease.[117] One commentator has referred to genetic tests for gene variants identified to have multiple, seemingly unrelated health effects as pleiotropic genetic tests.[118]

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[108] American Medical Association Council, "Multiplex Genetic Testing," 21; L. G. Biesecker and B. S. Wilfond, "Generic Consent for Genetic Screening," *New England Journal of Medicine* 331 (1994): 1024, 1024 (letter).

[109] S. Elias and G. J. Annas, "Generic Consent for Genetic Screening," *New England Journal of Medicine* 330 (1994): 1611, 1611–1612; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 275.

[110] Elias and Annas, "Generic Consent for Genetic Screening," 1612.

[111] Ibid.

[112] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 102.

[113] Ibid., 27, 102.

[114] See S. Elias and G. J. Annas, "Generic Consent for Genetic Screening," *New England Journal of Medicine* 331 (1994): 1025 (reply to letters about the original article).

[115] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 275.

[116] See Chapter 1, page 14.

[117] See E. T. Jeungst, "Caught in the Middle Again: Professional Ethical Considerations in Genetic Testing for Health Risks," *Genetic Testing* 1 (1997/1998): 189, 196; H. T. Greely, "Special Issues in Genetic Testing for Alzheimer Disease," *Genetic Testing* 3 (1999): 115, 117.

[118] See R. Wachtbroit, "The Question Not Asked: The Challenge of Pleiotropic Genetic Tests," *Kennedy Institute of Ethics Journal* 8 (1998): 131, 131. Pleiotropic genetic tests have also been called "versatile

Commentators disagree about the informed consent requirements for pleiotropic genetic tests. One commentator contends that providers have an obligation to disclose to patients the risks associated with learning information about all of the conditions detected by the tests.[119] This commentator also maintains that informed consent standards for a pleiotropic genetic test should be governed by the test's most "problematic use."[120] For example, because protocols for APOE testing for Alzheimer disease mandate the availability of pre- and posttest counseling, patient education, and patient support, cardiologists who perform APOE tests to determine cardiac disease risk for their patients should do so only if the counseling, education, and support are available.[121] This commentator recognizes that the inability of many cardiologists to satisfy the testing requirements of APOE testing's most problematic use might force the cardiologists to abandon such testing.[122]

Another commentator maintains that genetic counseling and other "special" clinical services are necessary to obtain informed consent only in the reproductive genetic testing context, where the historical concerns about eugenics are most prominent, or when there are

"special concerns" about the psychological state of the patient to be tested.[123] Accordingly, this commentator argues that, outside of these contexts, a provider who offers a patient a pleiotropic genetic test need only tell the patient about the different clinical uses of the test and need not provide any other special counseling or support services.[124]

Individuals who undergo pleiotropic genetic tests to learn about risks for particular disorders may not want to learn information about predispositions to other disorders that may be revealed by the tests. Because most commentators agree that predictive genetic testing should be voluntary[125] and that individuals have a "right not to know" their genetic information,[126] it follows that they would also agree that individuals have a right not to learn

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genetic tests" by one commentator. E. T. Jeungst, "Caught in the Middle Again," 196. For further discussion of pleiotropic genetic testing, see Chapter 3, page 76.

[119] Juengst, "Caught in the Middle Again," 196–197.

[120] Ibid.

[121] Ibid. See also Greely, "Special Issues in Genetic Testing," 118 (arguing that, given the weak association of APOE status and the risk of developing Alzheimer disease, patients who undergo APOE testing to learn their cardiac risks should be informed about the meaning of the results with regard to their Alzheimer risk only if they ask for them; if a patient does ask for the information, the physician, if able, should counsel the patient and provide the patient with a competent interpretation of the results if the patient still wants them or refer the patients to someone who can.).

[122] Ibid., 197.

[123] Wachtbroit, "The Question Not Asked," 139–140.

[124] Ibid.

[125] See, e.g., NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 12; American Society of Human Genetics, "Genetic Testing for Breast and Ovarian Cancer Predisposition," i.

[126] See, e.g., L. Andrews, "Body Science: As Medical Research Unlocks the Secrets of Genetics, the Battle Over Who Can Have Access to Your Personal Life Story Is Just Getting Under Way in Courts and Legislatures," *American Bar Association Journal* 83 (1997): 44, 45; K. A. Jensen, "Genetic Privacy in

all of the information revealed by pleiotropic genetic tests.[127] However, some commentators maintain that individuals' responsibility to family and loved ones can sometimes morally obligate them to learn their information.[128]

## Informed Consent for Storage and Research Use of Tissue Samples Obtained in the Clinical Context

For over a century, physicians and scientists have collected tissue samples and stored them in repositories.[129] Today, there are approximately 282 million stored tissue samples in the United States, the most common source of which are tissues collected during clinical medical procedures.[130] These stored samples are used by researchers as their principal source of human biological materials,[131] even though many of the patients from whom they were taken were not informed that their tissues would be stored and used for research.[132]

### Identified Tissue Samples

Identified tissue samples are samples that have names or other personal identifiers attached to them that permit researchers to directly identify the individual sources of the samples.[133] A National Institutes of Health/Centers for Disease Control and Prevention consensus workshop (the NIH/CDC workshop), the American College of Medical Genetics (ACMG), and the American Society of Human Genetics (ASHG) agree that informed consent should generally be required for the storage and research use of identified tissue samples obtained in the clinical context.[134] The ASHG and the NIH/CDC group maintain that blanket consents that permit researchers to use subjects' identified tissue samples for any genetic research projects in the future are inappropriate.[135]

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Washington State: Policy Considerations and a Model Genetic Privacy Act," *Seattle University Law Review* 21 (1997): 357, 364–365.

[127] See Greely, "Special Issues in Genetic Testing," 118.

[128] Wachtbroit, "The Question Not Asked," 142; R. Rhodes, "Genetic Links, Family Ties, and Social Bonds: Rights and Responsibilities in the Face of Genetic Knowledge," *Journal of Medicine and Philosophy* 23 (1998): 10.

[129] National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 1, 13.

[130] Ibid., 2.

[131] Ibid., 19

[132] Ibid., 6–7.

[133] Ibid., 17.

[134] American Society of Human Genetics, "ASHG REPORT: Statement on Informed Consent for Genetic Research," *American Journal of Human Genetics* 59 (1996): 471, 471–473 (discussing collection of tissue samples for research generally); Clayton et al., "Informed Consent for Genetic Research," 1791; American College of Medical Genetics, "ACMG Statement: Statement on Storage and Use of Genetic Materials," ACMG website: *http://www.faseb.org/genetics/acmg/pol-17.htm*, visited November 12, 1999.

[135] American Society of Human Genetics, "Statement on Informed Consent," 473. Clayton et al., "Informed Consent for Genetic Research," 1791.

Some commentators question whether the clinical setting, where subjects already have complicated matters to consider related to their medical treatment, is the appropriate environment in which to obtain informed consent for research on identified and identifiable tissue samples.[136] The National Bioethics Advisory Commission (NBAC) states that consent for future research use of an individual's tissue should be obtained separately from the consent process to the clinical procedure.[137] This could be accomplished by requesting consent for the research use of the samples before or after patients have provided consent for the clinical procedure.[138] The National Action Plan for Breast Cancer (NAPBC) recommends that patients should be given consent forms for the storage and use of tissue for research several days before their clinical procedures are to be performed.[139] Moreover, the NAPBC also emphasizes that patients should be informed that, no matter what decision they make regarding the use of their tissues for future research, their care will not be affected.[140]

**Anonymized Tissue Samples**

Anonymized tissue samples are samples whose identifiers have been removed and whose individual sources cannot be identified.[141] The samples may contain demographic data. The ASHG contends that it is unnecessary to obtain patients' consent to anonymize their tissue samples, to store the anonymized samples, or to use the anonymized samples in research.[142] In support of this position, some have argued that consent is not necessary because no harm can come to individuals who cannot be linked to the research.[143]

By contrast, the NIH/CDC workshop;[144] the ACMG;[145] numerous pathology organizations, including the College of American Pathologists (CAP);[146] and NBAC[147]

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[136] National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 63–64.
[137] Ibid., 63–65
[138] Ibid., 64.
[139] National Action Plan for Breast Cancer, "Model Consent Form for Biological Tissue Banking: Focus Group Report," National Action Plan for Breast Cancer, National Action Plan for Breast Cancer website: *http://www.napbc.org/napbc/model_consent.htm*, visited December 22, 1998.
[140] See National Action Plan for Breast Cancer, "Consent Form for Use of Tissue for Research," National Action Plan for Breast Cancer, National Action Plan for Breast Cancer website: *http://www.napbc.org/napbc/consent.htm*, visited December 24, 1998.
[141] National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 16–17.
[142] American Society of Human Genetics, "Statement on Informed Consent," 471–472.
[143] N. A. Holtzman and L. B. Andrews, "Ethical and Legal Issues in Genetic Epidemiology," *Epidemiology Review* 19 (1997): 163, 166. Holtzman and Andrews do not support this argument.
[144] Clayton et al., "Informed Consent for Genetic Research on Stored Tissue Samples," 1786.
[145] American College of Medical Genetics Materials Committee, "ACMG Statement on Storage and Use of Genetic Materials," *American Journal of Human Genetics* 57 (1995): 1499.
[146] W. Grizzle et al., "Recommended Policies for Uses of Human Tissue in Research, Education, and Quality Control," *Archives of Pathology and Laboratory Medicine* 123 (1999): 296, 299–300.
[147] National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 64–65.

contend that patient consent should be obtained in such circumstances. Some commentators who support this view argue that individuals can have valid reasons for not participating in research (for example, religious or cultural reasons) and that individuals can be harmed by stigma or discrimination if the results of the research are associated with the population group to which they belong.[148]

### Coded Tissue Samples

Coded tissue samples are tissue samples that are identified by codes and can be linked by a third party (a gatekeeper), who is not the researcher, to the individual sources of the samples.[149] The availability of coded samples for research enables researchers to perform longitudinal and other studies that are not possible using anonymized samples and could only otherwise be performed with identified samples. However, unlike anonymized samples, there is the potential for research results associated with coded samples to be linked to the patients and disclosed to third parties.[150] Even commentators who are concerned about this possibility maintain that strict confidentiality procedures should make the risk of such disclosures minimal.[151]

The NIH/CDC consensus workshop, the ACMG, NBAC, and the ASHG agree that informed consent should generally be required for research on coded tissue samples obtained in the clinical context.[152] By definition, studies that use coded tissue samples involve researchers obtaining through the gatekeeper health information from the subjects' medical records. NBAC contends that, in general, consent issues concerning the research uses of tissue samples and medical records are similar and that, as a general rule, research on tissue samples and medical records should be treated similarly.[153]

The ASHG and the NIH/CDC group maintain that "blanket consents that permit researchers to use subjects' coded tissue samples for any and all genetic research projects in the future are inappropriate."[154] Although NBAC contends that blanket consent for research on coded samples is generally appropriate, it adds that informed consent should

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[148] N. A. Holtzman and L. B. Andrews, "Ethical and Legal Issues in Genetic Epidemiology," *Epidemiology Review* 19 (1997): 163, 166; National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, vii; E. W. Clayton, "Panel Comment: Why the Use of Anonymous Samples for Research Matters," *Journal of Law, Medicine, and Ethics* 23 (1995): 375.

[149] National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 17.

[150] E. W. Clayton et al., "Informed Consent for Genetic Research on Stored Tissue Samples," *Journal of the American Medical Association* 274 (1995): 1786, 1787.

[151] Ibid.

[152] American Society of Human Genetics, "ASHG REPORT: Statement on Informed Consent for Genetic Research," *American Journal of Human Genetics* 59 (1996): 471, 471–473 (discussing collection of tissue samples for research generally); Clayton et al., "Informed Consent for Genetic Research," 1791; American College of Medical Genetics, "ACMG Statement: Statement on Storage and Use of Genetic Materials," ACMG website: *http://www.faseb.org/genetics/acmg/pol-17.htm*, visited November 12, 1999; National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 63–66.

[153] National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 74–75.

[154] American Society of Human Genetics, "Statement on Informed Consent," 473. See Clayton et al., "Informed Consent for Genetic Research," 1791.

be required if the research might be considered sensitive or objectionable, such as studies involving "certain behavioral genetic protocols" or "studies differentiating traits among ethnic or racial groups."[155] The Human Genome Organization (HUGO) recommends that coded tissue samples obtained from a patient during medical care may be stored and used for research if the patient was "generally notified" of the policy of using such samples for research and did not object and the samples have been coded.[156]

### Federal Regulations for the Protection of Human Research Subjects

Federal regulations dictate the manner in which research involving human research subjects that is federally funded, regulated, or performed by the federal government, including genetic research, may be conducted.[157] The federal regulations also cover all research performed by institutions that submit "Multiple Project Assurances" to the Office of Protection from Research Risks.[158] The regulations define research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge"[159] and cover research on living persons, identified and identifiable biological samples, and identified and identifiable medical records from living persons.[160] Research on deceased persons and on biological samples and medical records that are in the public domain or are anonymized by researchers are exempt from the regulations.[161] Moreover, under the regulations, researchers may take already-existing samples that contain identifiers and anonymize them without seeking the subjects' consent or approval by an IRB.[162]

The regulations require that persons conducting research on identified and coded tissue samples from living persons obtain the subjects' informed consent to the research and IRB approval.[163] The Office for Protection from Research Risks, which implements the regulations,[164] has indicated that researchers should use the process model of informed consent to obtain the subjects' consent.[165]

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[155] National Bioethics Advisory Commission, *Research Involving Human Biological Materials*, 74–75.
[156] The Human Genome Organisation (HUGO) Ethics Committee, "Statement on DNA Sampling: Control and Access," The Human Genome Organisation website: *http:// www.gene.ucl.ac.uk/hugo/sampling.html*, visited December 24, 1998.
[157] 45 C.F.R. § 46.101 (1999).
[158] 45 C.F.R § 46.103 (1999).
[159] 45 C.F.R. § 46.102(d) (1999).
[160] Ibid., § 46.102(f). See National Bioethics Advisory Commission, *Research Involving Human Biological Tissues*, 30, 35.
[161] 45 C.F.R. §§ 46.101(b)(4), 46.102(f).
[162] Ibid., §§ 46.101(b)(4), 46.102(f).
[163] See Office of Human Subjects Research, "Interim Guidance on the Research Use of Stored Samples or Data," Office of Human Subjects Research Website: *http://helix.nih.gov:8001/ohsr/info/ninfo_14.php3*, visited May 17, 1999. See 45 C.F.R. § 46.116 (1999).
[164] See Office for Protection from Research Risks, "Frequently Asked Questions about the Office of Protection from Research Risks (OPRR) and the Protection of Human Subjects of Research Supported by

The regulations permit research on identified or coded tissue samples from living persons with limited or no informed consent if an IRB determines that: "(1) [t]he research involves no more than minimal risk to the subjects, (2) [the lack of informed consent] will not adversely affect the rights and welfare of the subjects, (3) [t]he research could not practicably be carried out [with informed consent], and (4) [w]henever appropriate, the subjects will be provided with additional pertinent information after participation."[166]

**New York State Law on the Protection of Human Subjects**

Article 24-A of the New York Public Health Law regulates research on human subjects in New York State that is not regulated by the federal regulations.[167] Human research is defined as "any medical experiments, research, or scientific or psychological investigation, which utilizes human subjects and which involves physical or psychological intervention by the researcher upon the body of the subject" and are not performed for the subject's clinical benefit.[168] A human subject is defined as "any individual who may be exposed to the possibility of injury, including physical, psychological or social injury, as a consequence of participation as a subject in any research" which are greater than those experienced in daily life.[169] Article 24-A law prohibits "human research" on "human subjects" without the subjects' written informed consent.[170]

The law specifically excludes from its coverage research on body tissues and fluids after they have been removed "in the course of standard medical practice."[171] For example, a physician who obtains a blood sample from a patient to determine whether the patient has a virus and then subsequently uses the blood for biological research is not subject to Article 24-A.[172] Moreover, since the law requires a "human subject" to be an "individual who may be exposed to the possibility of injury, including physical, psychological, or social injury as a consequence of participation as a subject in any research,"[173] it arguably permits research on anonymous samples, samples from which the identifiers have been removed, and samples from deceased persons without informed consent.

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the U.S. Department of Health and Human Services," Office of Protection from Research Risks website: *http://www.nih.gov/grants/oprr/humansubjects/guidance/faqoprr.htm*, visited November 10, 1998.

[165] See Office for Protection from Research Risks, "Tips on Informed Consent," Office for Protection from Research Risks website: *http://www.nih.gov/grants/oprr/humansubjects/guidance/ictips.htm*, visited November 10, 1998. For a discussion of the process model of informed consent, see page 185, this chapter.

[166] 45 C.F.R. § 46.116(d)(1-4) (1999). See Office of Human Subjects Research, "Interim Guidance on the Research Use of Stored Samples or Data," Office of Human Subjects Research website: *http://helix.nih.gov:8001/ohsr/info/ninfo_14.php3*, visited May 17, 1999.

[167] N.Y. Pub. Health Law § 2445 (Mckinney 1999).

[168] Ibid., § 2441(2).

[169] Ibid., § 2441(1).

[170] Ibid., § 2442.

[171] Ibid., § 2441(2)

[172] See *Hecht v. Kaplan*, 221 A.D.2d at 104–105, 645 N.Y.S.2d at 53.

[173] N.Y. Pub. Health Law § 2441(1) (McKinney 1999).

Article 24-A requires that all human research be approved and monitored by a "human research review committee," such as an IRB.[174] All persons who conduct human research must affiliate themselves with an institution or agency that has such a committee.[175]

## Conclusions and Recommendations

### Necessity of Informed Consent for Predictive Genetic Testing in the Clinical Context

**Predictive genetic testing should not be performed without the informed consent of the subject of the test, except in the limited circumstances described below.**

Obtaining a patient's informed consent to medical procedures is both a legal requirement and a basic principle of medical ethics. Informed consent to predictive genetic testing is no exception. Unlike many medical procedures, however, most of the risks inherent in predictive genetic testing are not from the physical dangers of the procedure itself — which usually involves taking a blood or saliva sample and testing — but from the consequences of learning the information gleaned from the tests and of the information's potential disclosure. This poses a challenge to the traditional informed consent rubric, which, for the most part, focuses on informing the patients about the physical risks and benefits of, and alternatives to, particular procedures. Nonetheless, the basic purposes of informed consent — such as promoting patient autonomy, avoiding fraud and duress, and facilitating rational decision-making by patients[176] — apply with equal force in the predictive genetic testing context.

### Power of the Commissioner of Health

**New York law should be amended to authorize the Commissioner of Health to issue regulations on the process and content of informed consent to predictive genetic testing. Those sections of New York's existing genetic testing statutes that list specific elements of informed consent should be replaced with this general authorization.**

Advances in genetic testing are occurring at an explosive rate, and the complexity of the medical and psychosocial ramifications of such testing is increasing concomitantly. Detailed legislation on informed consent requirements for predictive genetic testing is insufficiently flexible to be responsive in this ever-changing environment. We believe that

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[174] Ibid., §§ 2444(1), 2444(2), 2444(3).
[175] Ibid., § 2444(2).
[176] B. R. Furrow et al., *Health Law: Cases, Materials and Problems*, 3d ed. (St. Paul, MN: West, 1997), 397.

the Commissioner of Health, with the expertise of the New York State Department of Health at his or her disposal, is in the best position to monitor developments in predictive genetic testing and to amend informed consent requirements as needed through regulation.[177] Thus, we recommend that New York's genetic testing statutes should be amended to replace the detailed list of required informed consent disclosures with general authorization for the Commissioner of Health to regulate the process and content of informed consent.

**Content of Informed Consent for Predictive Genetic Testing in the Clinical Context**

**Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predicative genetic testing, the Commissioner should require the following information to be provided to the patient before obtaining the patient's consent (elements currently not required by New York law are italicized).**

- **The purpose of the test**

  Providers should explain what the tests are designed to detect and why they are performing the tests. For example, patients undergoing BRCA1 testing would be told that the test detects specific genetic mutations that have been associated with a predisposition to breast cancer and that the test is being performed to determine whether the patient has such mutations.

- **A general description of the testing process**

  For example, if the testing procedure involves the drawing of blood, the provider should tell the patient about the needle puncture, the amount of blood to be drawn, and that the blood will be sent to a laboratory for testing. The patients also should be given a realistic timetable for learning the test results.

- **A description of the diseases or conditions tested for, *including their ranges of severity***

  To make an informed decision about whether to undergo a particular predictive genetic test, a patient needs to be informed about the disease or condition whose chances of occurring the test is designed to assess. The range of severity of the disease or condition is an important factor in deciding whether to undergo testing.

[177] For our recommendation on the creation of a genetics advisory committee by the Commissioner of Health, see Chapter 11, page 341.

- ***The risks and benefits of, and the alternatives to, the predictive genetic test***

  Information about the risks and benefits of, and alternatives to, medical procedures is an integral part of informed consent. The risks and benefits of a predictive genetic test should include not only the physical risks associated with the testing procedure, but also the psychosocial risks such as psychological distress from positive, negative, and indeterminate results; adverse use of the results in insurance and employment decisions; social stigma; learning incidental information about oneself and one's family (such as mispaternity); and unconsented-to disclosures of test results.[178] Examples of possible benefits are early detection and treatment of disease. An example of a possible alternative to predictive genetic testing is the use of empiric risk tables for estimating a patient's likelihood of developing a particular disease.

- **Confidentiality issues,** ***including confidentiality protections, the circumstances under which results of tests may be disclosed without the patient's consent,*** **and the names of the persons, categories of persons, and/or organizations to whom the patient has consented to disclose the results.**

  One of the greatest concerns that patients have about undergoing predictive genetic testing is that the test results will be disclosed to persons, such as employers and insurers, without the patient's consent. Health care providers should inform their patients about the confidentiality protections they provide for genetic information and that some persons or organizations, such as quality assurance reviewers and government inspectors, may have access to the patient's predictive genetic testing records without the patient's consent. Although health care providers should not be expected to provide legal advice, they should give their patients a general overview of the confidentiality protections provided by law for predictive genetic test results and refer them to appropriate government agencies or other professionals for more information.

- ***Protections against adverse uses of genetic information***

  Many patients are concerned that their predictive genetic test results may be used against them by employers and insurers, and as noted above, they

[178] For a more detailed discussion of the psychosocial risks associated with predictive genetic testing, see Chapter 3, pages 56 and 68.

should be informed about the risk of such uses. Health care providers should give their patients a general overview of the legal protections against the use of genetic information in insurance and employment decisions and refer them to appropriate government agencies or other professionals for more information.

- ***The chances of false positive and false negative results***

  All laboratory tests, including predictive genetic tests, are subject to some error.[179] Providers should explain to patients that predictive genetic tests are not always accurate and should inform patients about the rates of false positive and false negative results.

- **The meaning of both positive *and negative* results**

  New York law requires that, as part of informed consent to predictive genetic testing, health care providers explain the level of certainty that a positive test result serves as a predictor of the particular disease or condition tested for, that is, the test's clinical validity.[180] However, informing patients about the meaning of a negative test result is equally as important. In many circumstances in which healthy adults are tested to determine future disease risks, a negative result does not mean that the patient does not have a risk of developing a particular disease. It means only that the patient has not inherited the particular mutations the test is able to detect. The patient would still be at risk of developing the disease due to environmental factors or genetic factors not detected by the particular test.

- ***The ability, or lack thereof, of the test to predict the disease's severity and age of onset***

  Information about the limits of the predictive power of genetic tests is an important part of the process of informed consent. Many predictive genetic tests cannot predict the disease's severity, and/or the age of onset. Reproductive testing for Gaucher disease cannot determine where, along a broad range of severity, an individual's offspring may be affected

[179] See, e.g., N. A. Holtzman, *Proceed with Caution: Predicting Genetic Risks in the Recombinant DNA Era* (Baltimore: Johns Hopkins University Press, 1989), 92–93; Chapter 2, page 41 (discussion of analytical validity).

[180] For a discussion of clinical validity, see Chapter 2, page 41.

- ***The possibility that no additional risk information will be obtained at the completion of the test***

  In some circumstances, predictive genetic tests results may not reveal additional risk information. For example, BRCA1 tests can detect mutations within the BRCA1 gene whose possible effects on future health are not yet known. Chromosomal fetal cell analysis may disclose results of uncertain clinical significance. Patients who are contemplating predictive genetic testing should be informed about these sorts of possibilities.

- ***Available medical surveillance, treatment, and/or reproductive options following testing***

  Patients may make different decisions about undergoing predictive genetic testing depending on the availability of medical interventions or reproductive options following testing. Some patients might be more willing to take predictive genetic tests for conditions that are treatable than for those that are not. Similarly, for patients who are concerned that they may be carriers of genetic mutations that cause diseases in offspring, such as cystic fibrosis, the possibility of avoiding disease transmission through assisted reproductive technologies may be an important factor in some patients' decisions.

- **A statement that, prior to providing informed consent to genetic testing and after receiving the results, the individual may wish to obtain professional genetic counseling**

  Although the provider who orders a predictive genetic test has the responsibility to obtain the patient's informed consent and to explain the meaning of the test results, the provider should tell the patient that professional genetic counselors may be available to discuss the issues involved in greater depth. Health care providers should encourage patients to seek such counseling if it is available in the patient's community.

- ***The risks of transmitting the relevant mutation to children and that the mutation may be present in other blood relatives***

  A patient's decision about whether to undergo predictive genetic testing to learn about his or her own genetic disease risk may be affected by learning the risks of transmitting the relevant mutation to his or her children and that the mutation may be present in blood relatives. For example, some

patients might decline to undergo testing to avoid the responsibility of having to decide whether to disclose information about familial mutations to relatives.

- **A statement that no tests other than those authorized will be performed on the biological sample and that the sample will be destroyed at the end of the testing process, or not more than a specific period of time after the sample was taken, unless the subject consents to a longer period of storage.**

  Medical facilities should not be permitted to store an individual's biological samples without informed consent. Accordingly, in the predictive genetic testing context, the samples should be destroyed at the end of testing process or, at the very latest, at some specified period of time after the sample was taken, unless the person who provided the sample consents to a longer period of storage.

- ***That the test is voluntary***

  Patients should be told that they are under no obligation to undergo predictive genetic testing. Patients should also be told that they can request that the testing process end at any time and that providers will comply, and will use reasonable efforts to have the testing laboratories comply, with the request.

- ***An offer to answer inquiries***

  Patients should have the opportunity to talk with their health care providers about the predictive genetic tests they are considering, and they should be encouraged to ask questions.

- ***The fees charged for the laboratory tests and pre- and posttest counseling***

  Before consenting to predictive genetic testing, patients should be informed of its cost, as well as any additional costs associated with counseling.

**Sufficiency of Signed Informed Consent Form as Evidence of Informed Consent**

**Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require that health care providers disclose the information described above in a manner that**

**will enable the patient to make a knowledgeable evaluation. A signed informed consent form is not necessarily sufficient evidence that this goal has been achieved.**

Obtaining informed consent to medical procedures involves more than having patients sign informed consent forms. Health care providers must communicate information to patients in a manner that allows the patients to make a knowledgeable evaluation. While New York's general law on informed consent to medial procedures mandates this standard of communication, New York's genetic testing laws could be interpreted to define informed consent as merely a signature on an informed consent form.[181] We believe that the standard of communication for informed consent to testing should be made consistent with the standard that applies to medical procedures generally.

**Use of Decision Aids in the Informed Consent Process**

**Health care providers are encouraged to use decision aids, such as written materials, videos, group discussions, and CD-ROMs, as part of the informed consent process to predictive genetic testing. However, health care providers should not use decision aids as a substitute for discussing predictive genetic testing issues with their patients.**

Decision aids such as videos and written materials have been shown to help patients make more informed decisions about undergoing medical treatments.[182] The use of decision aids in the predictive genetic testing context appears to have a similar effect.[183] In view of the complexity of the information that patients must weigh in

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[181] See page 183, this chapter.

[182] See A. M. O'Connor et al., "Decision Aids for Patients Facing Health Treatment or Screening Decisions: Systematic Review," *British Medical Journal* 319 (1999): 731; A. Edwards and G. Elwyn, "The Potential Benefits of Decision Aids in Clinical Medicine," *Journal of the American Medical Association* 282 (1999): 779.

[183] See G. McGee and C. Malik, "New Media: Breast Cancer Counseling," *Journal of the American Medical Association* 281 (1999): 1652, 1652 (positive review of CD-ROM program to aid in informing patients about genetic testing for predisposition to breast cancer); A. Cull et al., "The Use of Videotaped Information in Cancer Genetic Counseling: A Randomized Evaluation Study," *British Journal of Cancer* 77 (1998): 830 (1998) (videotape); B. Cheuvront et al., "Psychosocial and Educational Outcomes Associated with Home- and Clinic-Based Pretest Education and Cystic Fibrosis Carrier Testing among a Population of At-Risk Relatives," *American Journal of Medical Genetics* 75 (1998): 461 (use of educational pamphlet at home); C. Lerman et al., Controlled Trial of Pretest Education Approaches to Enhance Informed Decision-Making for BRCA1 Gene Testing," *Journal of the National Cancer Institute* 89 (1997): 148 (comparing an "educational" approach to pretest education with an educational plus counseling approach). See also M. J. Green and N. Fost, "Who Should Provide Genetic Education prior to Gene Testing? Computers and Other Methods for Improving Patient Understanding," *Genetic Testing* 1 (1997): 131 (proposing the use of computer-based education for patients considering genetic testing); M. J. Green and N. Fost, "An

deciding whether to undergo predictive genetic testing, we encourage health care providers to use decision aids as part of the informed consent process. However, decision aids cannot replace actual interaction between health care providers and their patients, and health care providers should not use decision aids as a substitute for discussing predictive genetic testing issues with their patients.

**Persons Required to Obtain Informed Consent**

**Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require that the person who orders a predictive genetic test has the obligation to ensure that the subject's informed consent is obtained.**

New York's genetic testing law currently prohibits the *performance* of predictive genetic tests on biological samples without the subject's prior written informed consent. However, it is the health care provider who orders the test[184] — not the laboratory that performs it — who interacts with the patient and is responsible for the quality of the patient's care. Accordingly, it should be the responsibility of the health care provider to obtain the subject's informed consent.

**Responsibility of Testing Laboratories**

**The New York State Department of Health should permit clinical laboratories to perform predictive genetic tests on biological samples only if the laboratories receive assurances that the subjects provided informed consent for the tests.**

Genetic testing laboratories currently perform virtually all predictive genetic testing and can play an important role in helping to ensure that informed consent for the testing has been obtained. Under its authority to regulate laboratories,[185] the New York State Department of Health should prohibit licensed laboratories from performing predictive genetic tests on biological samples unless the laboratories have received assurances from the persons ordering the tests that the subjects have provided informed consent for the tests. The department should issue regulations describing the nature of the assurances that the laboratories need to obtain. In the absence of such assurances, laboratories should stabilize the specimens and contact the providers to determine

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Interactive Computer Program for Educating and Counseling Patients about Genetic Susceptibility to Breast Cancer," *Journal of Cancer Education* 12 (1997): 204 (discussing a CD-ROM developed to help patients decide whether to undergo genetic testing for breast cancer susceptibility).

[184] See 10 NYCRR § 58-1.7(b) (1999) (listing persons who are authorized to submit biological samples to clinical laboratories for diagnostic testing).

[185] For a discussion of the New York State Department of Health's power to oversee laboratories, see Chapter 11, page 321.

whether informed consent has been or can be obtained. The providers should bear the expense of the samples' stabilization.

### Professional Guidelines on the Process and Content of Informed Consent for Predictive Genetic Tests

**Professional organizations should issue guidelines on the process and content of informed consent for specific predictive genetic tests and should create model consent forms that are consistent with existing law and contain the information necessary for patients to make informed decisions about undergoing predictive genetic testing.**

Given the variety and number of predictive genetic tests, general guidelines on the content and process of informed consent to such tests are helpful, but have only limited utility. Professional organizations, such as the American Society of Human Genetics, have the collective expertise to draft detailed informed consent guidelines for specific predictive genetic tests, and we recommend that they do so.

### Health Care Providers Qualified to Order Predictive Genetic Tests

**Health care providers should order predictive genetic tests only when (1) they know the circumstances under which it is appropriate to order them and the meaning of their results, (2) they are capable of providing their patients with sufficient information to make informed decisions about undergoing the tests, and (3) they are able to provide their patients with comprehensive pre- and posttest counseling or can refer their patients to professionals who are able to do so.**

As predictive genetic testing becomes more prevalent, physicians who are not genetic specialists will increasingly be called upon to make recommendations to their patients about such testing. At present, physicians appear to be cautious about ordering predictive genetic tests.[186] This caution is commendable, as most physicians are not sufficiently proficient in genetics to know the proper circumstances for ordering predictive genetic tests, the meaning of genetic test results, and the method for explaining the results to their patients. We believe that only health care providers who have such knowledge should order predictive genetic tests.

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[186] See V. Foubister, "Lapses in Practice, Oversight Undercut Genetic Testing," *American Medical News*, October 18, 1999, 8, 10.

### Informed Consent to Multiplex Genetic Testing

**Ideally, a patient's full informed consent should be obtained to each test on a multiplex panel prior to testing. However, generic consent to multiplex testing is appropriate if (1) the number of tests on the panel is so high or the information about the tests is so complicated that attempting to obtain full informed consent from the patient to each test would be confusing or otherwise burdensome to the patient; (2) the tests on the panel meet all of the criteria described in Chapter 5 for inclusion in a multiplex panel; (3) the patients are informed, prior to testing, that more detailed information about each test is available; and (4) the patients are given an opportunity to obtain that information prior to testing either from the health care provider offering the multiplex panel or from another health care professional. Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should permit generic consent to multiplex genetic testing under these circumstances.**

As the number of tests physicians use in routine clinical practice grows, it will become difficult as a practical matter for physicians to provide patients with detailed information about all of the tests they offer. In addition, the utility of giving patients all of this information is questionable since information overload may prevent the patients' consent from being truly informed.

As discussed in Chapter 5, multiplex panels should be limited to genetic tests (1) that have a high level of analytical validity, clinical validity, and clinical utility; (2) whose results will not have significant psychosocial ramifications; and (3) to which the vast majority of people would consent if they were fully informed.[187] It is appropriate to use generic consent for multiplex genetic testing if these criteria are satisfied.

The generic consent process would highlight broad concepts and common-denominator issues for all the tests.[188]

### Special Issues Related to Pleiotropic Information

**Before offering a predictive genetic test to a patient, providers should give the patient all information necessary for the patient to provide informed consent to the intended use of the test, that is, information relevant to any condition about which the patient intends to receive test results. If the test also may reveal confirmed, clinically valid information about conditions for which the patient has not sought**

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[187] See Chapter 5, page 138.

[188] Elias and Annas, "Generic Consent for Genetic Screening," 1612.

**testing, the provider should inform the patient of this fact, specifying (1) the condition(s) about which the test may reveal information; (2) the consequences of having this additional information in his or her medical record; and (3) opportunities, including genetic counseling, for the patient to obtain further information about aspects of the test unrelated to its intended use. If the patient expresses an interest in learning how his or her test results relate to conditions for which testing was not originally sought, the provider should ensure that the patient provides informed consent to obtaining this additional information. Providers should respect patients' right not to learn pleiotropic information revealed by genetic tests.**

Information about multiple health conditions sometimes will be an unwanted by-product of genetic testing. For example, testing for a particular variant of the APOE gene may help guide treatment for coronary artery disease, but some variants also have been associated with an increased risk for late-onset Alzheimer disease. Because there are currently no treatments for Alzheimer disease, patients who undergo an APOE test for purposes of cardiac treatment may not want to learn how their test results relate to their risk of developing Alzheimer disease. Providers should respect the wishes of patients not to learn this unwanted information.

However, in order to ensure that patients understand the consequences of undergoing genetic tests that may reveal pleiotropic information, physicians should inform their patients, prior to testing, about the possibility that the test may reveal information about conditions for which the patients have not sought testing. Providers also should warn their patients about the consequences of having this information in their medical records, including the possibility that the information may be used against them by insurers or employers.

If the patient expresses an interest in learning how his or her test results relate to conditions for which testing was not originally sought — for example, if a patient undergoing an APOE test to guide treatment for coronary artery disease expresses an interest in learning how her test results affect her risk of developing Alzheimer disease — the patient should be fully informed of the risks and benefits of learning this additional information. Physicians unable to do this should refer the patient to other health care professionals who can.

**Professional organizations should create guidelines about informed consent to genetic tests that reveal pleiotropic information.**

### Court Orders for Predictive Genetic Testing

**New York law should be amended to permit courts to order predictive genetic testing without the subject's consent only when (1) absent the testing, there would be a clear and imminent danger to the public health; (2) such testing is authorized by federal and/or New York State statutes or regulations; or (3) in a civil or criminal litigation, the subject affirmatively places his or her physical or mental condition at issue and the predictive genetic testing directly relates to that physical or mental condition.**

New York law currently permits courts to issue orders compelling predictive genetic testing after weighing "the privacy interests of the individual subject of the genetic test and of close relatives of such individual," as well as "the public interest."[189] This test is too permissive and malleable and does not sufficiently take into account the common law, statutory, and constitutional right of individuals to refuse to undergo medical procedures.[190] In place of this standard, we recommend that court-ordered predictive genetic testing should be permitted only in the circumstances listed above.[191]

### Private Civil Remedies for the Performance of Predictive Genetic Testing without Informed Consent

**New York law should be amended to expressly authorize private lawsuits by subjects of unconsented-to predictive genetic tests against persons who order and/or perform the tests. In cases where the tests are performed without consent due to negligence, the subjects should be authorized to recover actual damages for physical, emotional, and/or financial harms they suffer as a result. In cases where the tests are performed with knowledge that no informed consent has been obtained or are performed without consent due to recklessness, victims should be authorized to recover actual damages for physical, emotional, and/or financial harms; punitive damages (in appropriate cases); and attorneys' fees. In cases where the unconsented-to testing is ordered and/or performed willfully (i.e., with knowledge that testing without informed consent is illegal), the subjects should be authorized to recover statutory damages even without proof of actual damages. New York law also should be amended to permit individuals to obtain injunctive relief to prevent unconsented-to predictive genetic testing and unauthorized use and/or retention of the results of such testing.**

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[189] See page 184, this chapter.

[190] See page 179, this chapter.

[191] An example of when genetic testing is required by statute is New York's newborn screening law. See N.Y. Pub. Health Law §2500-a (McKinney 1999); Chapter 5, page 149.

Subjecting individuals to predictive genetic testing without their informed consent violates their privacy and personal autonomy. In addition, the results of such testing could be used against them by insurers and others. The $1,000 and $5,000 fines currently authorized in the genetic testing statutes are too low to serve as effective deterrents, and, in any event, outside of the insurance context, they may be recovered by the state only if the violations are proven beyond a reasonable doubt.

We believe that individuals who have been subjected to predictive genetic testing without their consent should be compensated for the damages they suffer as a result. Because it is currently unclear whether New York law allows for such recovery, we recommend that New York law be amended to authorize it in cases where the failure to obtain informed consent was a result of negligence. Individuals who intentionally order or perform predictive genetic testing knowing that no informed consent has been obtained, or do so recklessly, are more culpable, and therefore should be subject to punitive damages in appropriate cases. Persons who know that informed consent has not been obtained for predictive genetic testing and perform it knowing that such testing is illegal, or persons who, for financial gain, intentionally or recklessly perform predictive genetic testing without informed consent should be subject to statutory damages as well. Statutory damages should be set high enough to dissuade individuals from violating the informed consent requirements of the genetic testing statutes. The standard of proof for recovery should be a preponderance of the evidence.

**Power of the Attorney General**

**New York law should be amended to authorize the Attorney General to bring lawsuits on behalf of individuals who have undergone predictive genetic testing without informed consent. New York law also should authorize the Attorney General to bring lawsuits to prevent such unconsented-to testing. The Attorney General should be empowered to seek whatever relief individuals could seek if they brought the lawsuits themselves.**

Individuals may not have the resources to bring lawsuits to protect their informed-consent rights under New York's genetic testing statutes. Because society as a whole benefits from the vigorous enforcement of informed consent protections, the Attorney General, as New York's chief legal officer, should have the authority to bring lawsuits on behalf of those unable or unwilling to sue themselves.

**Professional Discipline and Other Sanctions for Performing Predictive Genetic Tests without Informed Consent**

**Persons and organizations licensed by New York State should be subject to professional discipline and/or other sanctions, including fines and license suspension and revocation, for performing or ordering predictive genetic testing without informed consent.**

Individuals and organizations who are licensed or certified by New York State, such as physicians, insurance companies, and health care organizations, are expected to follow the law. The possible suspension or loss of a license for performing predictive genetic testing without obtaining informed consent can act as a powerful deterrent against such violations. Moreover, like actions by the Attorney General, disciplinary proceedings provide a mechanism for enforcing the informed consent provisions of the genetic testing laws that does not depend on the willingness of private parties to pay the costs associated with litigation.

**Research on Tissue Samples Obtained in the Clinical Setting**

**New York's law on the protection of human research subjects should be amended to cover research on tissue samples obtained in the clinical context. The amendment should apply only to tissue obtained after the amendment's effective date.**

Unlike the federal regulations, New York's law on the protection of human research subjects applies only to tissue samples obtained specifically for research, not to samples obtained in the clinical context. Because concerns about individual autonomy and inappropriate disclosure of research results apply in both situations, the law should be amended to cover tissue samples regardless of the tissue's origin.

**Research Use of Identified Tissue Samples Obtained in the Clinical Context**

**New York's laws on human subject research should be amended to permit research on identified tissue samples obtained in the clinical context only after the subjects have provided full informed consent to the research and an institutional review board has reviewed and approved the research protocol. The amendment should apply to all tissue obtained after the amendment's effective date.**

Because the results of research on identified tissue samples will directly be linked to patients, such research should only be permitted after the subjects have provided their full informed consent to specific research projects that will use their identified samples.[192]

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[192] New York's genetic testing statutes require full informed consent to genetic testing in the research context. See page 183, this chapter.

**Research Use of Anonymized Tissue Samples Obtained in the Clinical Context**

**New York's laws on genetic testing and the protection of human research subjects should be amended to permit research on anonymized tissue samples obtained in the clinical context only after an institutional review board has reviewed and approved of the protocols of such research. The institutional review board review should ensure that the samples are or will be truly anonymized and should determine whether the research is of such a sensitive nature that it is inappropriate to use anonymized samples without having obtained the subjects' specific consent to the research. The amendment should apply to all tissue obtained after the amendment's effective date.**

Research on human tissue samples obtained in the clinical setting has brought about great advances in medicine, and society has a strong interest in ensuring that such research continues. Because of the possibility of group harms arising from research results,[193] and out of respect for the individual autonomy of patients,[194] some commentators maintain that tissue samples obtained in the clinical context should be used for research only if the health care provider has obtained the patient's consent to such use — even if the sample will be fully anonymized.[195]

While we are sympathetic to these concerns, we believe that requiring patient consent to the use of tissue samples in anonymized research is not the best way to balance the competing interests at stake. First, for a consent requirement to be effective, systems would have to be developed to ensure that researchers use only those samples for which documentation of the patient's consent exists. This would mean that all tissue samples obtained in the clinical setting would have to be accompanied by written consent forms, and laboratories would have to segregate samples for which consent to future research use was not obtained. Such systems would impose tremendous administrative burdens, particularly for routine procedures, such as blood draws, where obtaining written consent is not currently standard practice. Because clinicians, who are generally not researchers, would have little incentive to comply with these administrative requirements, it is likely that many tissue samples obtained in the clinical setting would be stored without proper documentation; these samples would then be unavailable for subsequent research use. The result, therefore, of requiring patient consent to the use of tissue samples in

[193] For a discussion of group harms, see Chapter 3, page 72.
[194] See E. W. Clayton, "Panel Comment: Why the Use of Anonymous Samples for Research Matters," *Journal of Law, Medicine and Ethics* 23 (1995): 375, 376.
[195] Ibid.

anonymized research would be that the pool of samples available to researchers might decrease substantially, which could seriously jeopardize the ability to perform large-scale epidemiological studies.

At the same time, requiring patient consent to the use of tissue samples in anonymized research would do little to protect individual rights. By definition, the results of anonymized research cannot be linked to the sources of the tissue samples, so use of the tissue cannot lead to direct individual harm. While it is possible that anonymized research will lead to group harms, such as stigma based on membership in a particular ethnic category, few patients will be aware of this possibility unless they are given substantial information about the nature of genetic research — something that is unlikely to happen in the routine clinical encounter. Thus, requiring individual patient consent to anonymized tissue research would do little to prevent stigmatizing group research from taking place.

In light of the significant benefit of research to society, and our belief that most patients would consent to the research use of their tissues samples if all identifying information is removed, we believe that consent to the research use of tissue samples obtained in the clinical setting should be presumed if the samples will be anonymized before the research. To protect the interests of patients as both individuals and members of groups, such research should not proceed without the approval of an IRB. Before approving anonymized research with tissue samples obtained in the clinical setting, the IRB should determine (1) that the samples are or will be truly anonymized and (2) that the use of samples for which specific subject consent has not been obtained is appropriate, given the nature and potential consequences of the particular protocol. In making this second determination, the IRB should consider the possibility of group harms associated with the research, as well as whether the research involves particularly sensitive issues (e.g., research on cloning) about which it is inappropriate to presume that most subjects would consent if fully informed.

If a patient objects to the use of his or her tissue sample for anonymized research, providers and researchers should make a good faith effort to comply.

**Research Use of Coded Tissue Samples Obtained in the Clinical Context**

**New York's laws on human subject research and genetic testing should be amended to permit research on coded tissue samples obtained in the clinical context only if (1) the patients have agreed to the storage and research use of their coded samples; (2) the patients have been told about the operation, tissue release policies, and confidentiality protections of the tissue repository; and (3) an institutional review board has reviewed and approved of the protocols of such research. The institutional review board review should ensure that the samples are or will be truly coded and should determine whether the research is of such a sensitive nature that it is**

**inappropriate to use coded samples without having obtained the subjects' specific consent to the research. The coding of the samples should be performed by a person who is not connected to the research and who will not learn the individual results of the testing. That person should have the sole authority to use the codes to obtain patient information, other than identifying information, for the researchers. The amendment should apply to all tissue obtained after the amendment's effective date.**

Because of the possibility, however remote, that coded tissue samples could be linked to patients, we believe that requiring patient consent to such research is appropriate. However, given the nature of coded research, a requirement of full informed consent to every genetic test or research project should not be required.

Unlike identified samples, appropriately coded samples sufficiently protect the identity of individuals so that they will rarely, if ever, be subject to individual harms as a result of research. Thus, we believe that individuals should be given the option of providing a general authorization for the future use of their tissue samples in coded research. Before providing such consent, the patients should be told about the operation, tissue release policies, and confidentiality protections of the tissue repositories where the samples will be stored.

To protect the interests of patients as both individuals and members of groups, such research should not proceed without the approval of an IRB. Before approving coded research with tissue samples obtained in the clinical setting, the IRB should determine that (1) the samples are or will be truly coded; and (2) the use of samples for which specific subject consent has not been obtained is appropriate, given the nature and potential consequences of the particular protocol. As an additional protection of the patients' anonymity, the coding of the samples should be performed by a person who is not connected to the research and who will not learn the individual results of the testing. That person should have the sole authority to use the codes to obtain patient information, other than identifying information, for the researchers.

This system respects individual autonomy because patients are fully informed about the protections the repository affords their coded samples and have the ability to prohibit research on the samples. At the same time, it enables researchers to perform longitudinal and other studies that are not possible using anonymized samples and could only otherwise be performed with identified samples.

**Voluntariness of Participation in Research on Tissue Samples Obtained in the Clinical Context**

**Patients should be informed that their decision about whether to consent to the research use of their coded and/or identified tissue**

**samples is wholly voluntary and that their decision will not affect their access to or quality of care.**

Consent to the research use of coded and/or identified tissue samples obtained in clinical procedures should be entirely voluntary. Patients should be informed that their decision about whether to consent to the research use of such samples is wholly voluntary and that their decision will not affect their access to or quality of care.

### Encouraging Patient Authorization for the Use of Tissue Samples for Research

**Institutions should encourage clinicians to ask patients to consider authorizing the use of their tissue for research purposes, and clinicians should do so when they deem it appropriate.**

The availability of tissue samples is crucial for continued medical and scientific research. Although we recommend that institutions encourage physicians to ask patients to consider donating tissue samples, we emphasize that physicians should not do so in a coercive manner.

# 8

# Predictive Genetic Testing of Children

When susceptibility to a genetic disorder is discovered within a family, parents may seek predictive genetic testing of their minor children. Parents may request testing to obtain a medical benefit for the child, to reduce uncertainty about the child's future disease risk, and/or to make life-planning decisions. In some cases, adolescent children may seek testing themselves, generally to make life-planning decisions and "to consolidate a developing self-identity regarding work or parenthood."[1] For genetic susceptibility or carrier testing, the same benefits and risks associated with testing of adults apply,[2] but they may have different ramifications when the person tested is a minor. Additional concerns relate to issues of parental autonomy versus the future autonomy of the minor and questions about the minor's capacity and role in the decision-making process.[3]

[1] D. C. Wertz, J. H. Fanos, and P. R. Reilly, "Genetic Testing for Children and Adolescents: Who Decides?" *Journal of the American Medical Association* 272 (1994): 875.

[2] See page 221, this chapter.

[3] See page 226, this chapter.

## Requests for Predictive Testing of Children and Adolescents

Requests to perform genetic testing of healthy children to determine carrier status or future risk for late-onset disorders are not rare. For example, 44 percent of 1,084 surveyed genetics service providers in the United States reported that they had received requests to test children for adult-onset disorders.[4] In a national survey of 105 laboratories that perform DNA-based genetic testing, the majority of laboratories that offered presymptomatic testing for one or more of twelve late-onset disorders, including Huntington disease and familial colon cancer, reported that they had received requests for testing of healthy children or adolescents.[5] A majority of laboratories that offered carrier testing for one or more of six recessive disorders, including cystic fibrosis, received requests for testing of healthy children age twelve or younger.[6]

Surveys of the public and of health care providers indicate support for parental control over decisions about predictive testing of minor children. In one survey, 53 percent of adults thought parents should be able to have their children tested "for genetic conditions that may appear later in life" even if the conditions tested for were not preventable or treatable and even if testing "might lead to emotional problems or cause people to be prejudiced against the child."[7] In two surveys of women at increased risk for breast cancer due to family history, one-third or more of those surveyed thought parents should be able to test their minor children for inherited BRCA gene mutations.[8] A survey of physicians and nurse practitioners obtained a similar result: Over one-third of each

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[4] D. C. Wertz, "Society and the Not-So-New Genetics: What Are We Afraid Of? Some Predictions from a Social Scientist," *Journal of Contemporary Health and Law Policy* 13 (1997): 299.

[5] D. C. Wertz and P. R. Reilly, "Laboratory Practices for the Genetic Testing of Children: A Survey of the Helix Network," *American Journal of Human Genetics* 61 (1997): 1163, 1164–1165. With the exception of testing for Huntington disease — a nonpreventable, nontreatable, neurodegenerative adult-onset disorder that is virtually 100 percent penetrant — few laboratories reported ever refusing to perform a test based on the age of the patient. For some disorders included in the survey, such as familial colon cancer, testing prior to the age of majority may have a medical benefit.

[6] Ibid., 1165–1166.

[7] Wertz, "Society and the Not-So-New Genetics," 303 (citing results of a Roper-Starch Worldwide survey of 988 adults). See also D. C. Wertz, "Testing Children: Current Trends," *GeneLetter* (July 2000), website: *http:// www.geneletter.com*, visited July 17, 2000.

[8] J. L. Beckendorf et al., "Patients' Attitudes about Autonomy and Confidentiality in Genetic Testing for Breast-Ovarian Cancer Susceptibility," *American Journal of Medical Genetics* 73 (1997): 296, 298; G. Geller et al., "Decision-Making about Breast Cancer Susceptibility Testing: How Similar Are the Attitudes of Physicians, Nurse Practitioners, and At-Risk Women?" *Journal of Clinical Oncology* 16 (1998): 2868. Beckendorf et al. report that 88 percent of 238 unaffected women who had at least one first-degree relative with breast and/or ovarian cancer agreed that parents should be able to consent to susceptibility testing on behalf of their minor children. Geller et al. surveyed 426 women at increased cancer risk due to family history; 37 percent supported testing a thirteen-year-old daughter of a BRCA mutation carrier.

group supported predictive genetic testing of a thirteen-year-old daughter of a mother identified to have a BRCA gene mutation.[9]

## Legal Background

### Authority of Minors to Consent to Medical Treatment

In general, the common law and state statutes prohibit physicians from treating or performing medical procedures on minors without parental consent.[10] However, there are exceptions to this rule. For example, many states permit "emancipated minors" to make their own health care decisions. An emancipated minor is a minor "whose parents have completely surrendered care, custody, and control of the child, have no involvement in the child's earnings, and have renounced parental duties."[11] Emancipated minors generally include minors who are gainfully employed and fully self-supporting, minors who are married, and minors who enter military service.[12]

A number of states also permit "mature minors" to make their own medical decisions. A mature minor is a minor who "has the capacity to appreciate the nature and risks involved of the procedure to be performed, or the treatment to be administered or withheld"[13] and is "mature enough to exercise the judgment of an adult."[14] For example, in *Cardwell v. Bechtol*,[15] the Tennessee Supreme Court held that it was appropriate for a doctor to have treated a seventeen-year, seven-month-old woman for back pain without parental consent because she was mature enough to consent to the treatment.[16] In reaching its decision, the court applied what it termed the "Rule of Sevens," which states that minors below the age of seven rarely, if ever, have the capacity to consent to medical treatment, minors between the ages of seven and fourteen are presumed not to have the capacity to consent to medical treatment, although that presumption is rebuttable, and minors between the ages of fourteen and eighteen are presumed to have the capacity to consent to medical treatment, although that presumption is rebuttable as well.[17]

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[9] Geller et al., "Decision-Making about Breast Cancer Susceptibility Testing," 2868.
[10] See D. R. Veilleux, "Medical Practitioner's Liability for Treatment Given Child without Parent's Consent," 67 A.L.R.4th 511 (Rochester, NY: The Lawyers Co-operative, 1989 & Supp. 1998).
[11] See J. A. Penkower, "The Potential Right of Chronically Ill Adolescents to Refuse Life-Saving Medical Treatment — Fatal Misuse of the Mature Minor Doctrine," *DePaul Law Review* 45 (1996): 1165, 1177 (internal quotation marks omitted); New York State Task Force on Life and the Law, *When Others Must Choose: Deciding for Patients without Capacity* (New York: New York State Task Force on Life and the Law, 1992), 42–43.
[12] New York State Task Force on Life and the Law, *When Others Must Choose*, 43.

[13] *Belcher v. Charleston Area Med. Ctr.*, 188 W. Va. 105, 116, 422 S.E.2d 827, 838 (1992). See *In re E.G.*, 133 Ill.2d 98, 111, 549 N.E.2d 322, 328 (1989).
[14] *In re E.G.*, 133 Ill.2d at 111, 549 N.E.2d at 328. See *Belcher v. Charleston Area Med. Ctr.*, 188 W. Va. at 116, 422 S.E.2d at 838.
[15] 724 S.W.2d 739 (Tenn. 1987).
[16] Ibid., at 755.
[17] Ibid., at 749, 755.

Section 2504 of the New York Public Health Law generally prohibits minors (individuals under the age of eighteen) from obtaining medical care without the consent of their parents.[18] However, Section 2504 authorizes minors who are married, pregnant, or parents themselves to make their own medical decisions.[19] In addition, other New York statutes authorize minors to consent to particular medical treatments, including outpatient mental health services, treatment for sexually transmitted diseases, and treatment for substance abuse.[20]

The majority of cases involving emancipated minors in New York concern parental responsibility for continued child support.[21] Only one New York case has held that an emancipated minor may consent to medical treatment,[22] and that case was decided prior to the enactment of Section 2504. In addition, only one New York court has ever discussed the mature minor doctrine.[23] Although the court recommended that the legislature or the appellate courts adopt the mature minor doctrine in New York, it found that the minor in that case would not qualify as a mature minor even if the doctrine were recognized.[24] Because Section 2504 and other New York statutes specifically enumerate the circumstances under which minors may consent to health care without parental consent and do not (with possibly one exception)[25] explicitly recognize the mature minor or emancipated minor doctrines, it is unclear whether courts in New York have the power to recognize these doctrines without new legislation.[26]

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[18] See N.Y. Pub. Health Law § 2504(1) (McKinney 1999); *Alfonso v. Fernandez*, 195 A.D.2d 46, 50–51, 606 N.Y.S.2d 259, 262 (N.Y. App. Div. 1993); *Matter of Thomas B.*, 152 Misc.2d 96, 98–99 574 N.Y.S.2d 659, 660–661 (N.Y. Fam. Ct. Cattaraugus Cty. 1991).

[19] N.Y. Pub. Health Law § 2504(1) (McKinney 1999).

[20] See, e.g., N. Batterman, "Under Age: A Minor's Right to Consent to Health Care," *Touro Law Review* 10 (1994): 637, 657–659 (discussing New York statutes); *Matter of Long Island Jewish Medical Center*, 147 Misc.2d 724, 729–730, 557 N.Y.S.2d 239, 243 (N.Y. Sup. Ct. Queens Cty. 1990) (same).

[21] Batterman, "Under Age," 646; J. R. Brandes and C. L. Weidman, "The Age of Majority and Emancipation," *New York Law Journal*, June 28, 1994, 3.

[22] See *Bach v. Long Island Jewish Hosp.*, 49 Misc.2d 207, 267 N.Y.S.2d 289 (N.Y. Sup. Ct. Nassau Cty. 1966); Batterman, "Under Age," 648–650.

[23] *Matter of Long Island Jewish Med. Ctr.*, 147 Misc.2d 724, 557 N.Y.S.2d 239 (N.Y. Sup. Ct. Queens Cty. 1990).

[24] Ibid., 147 Misc.2d at 730, 557 N.Y.S.2d at 243.

[25] New York's statute governing HIV/AIDS testing and disclosure of test results appears to utilize the mature minor doctrine. It defines "capacity to consent" as "an individual's ability, determined without regard to the individual's age, to understand and appreciate the nature and consequences of a proposed health care service, treatment or procedure, or of a proposed disclosure of confidential HIV related information, as the case may be, and to make an informed decision concerning the service, treatment, procedure or disclosure." N.Y. Pub. Health Law § 2780(5) (McKinney 1999).

[26] See Batterman, "Under Age," 641, 644–660 (discussing whether the mature minor and emancipated minor doctrine survived the enactment of Section 2504). See generally *Fumarelli v. Marsam Dev., Inc.*, 92 N.Y.2d 298, 680 N.Y.S.2d 440 (1998) (describing the method for determining whether a statutory enactment supersedes the common law). At least two courts in other states have utilized the mature minor

## Authority of Parents to Control Their Children's Medical Care

New York courts accord great deference to parental choices about medical care for their children[27] and will intervene only when the parents' choices seriously jeopardize a child's health or welfare.[28] The test for determining whether parental decisions will be upheld is whether the parents, "having sought accredited medical assistance and having been made aware of the seriousness of their child's affliction and possibility of cure if a certain mode of treatment is undertaken, have provided their child a treatment which is recommended by their physician and which has not been totally rejected by all responsible medical authority."[29]

For example, in *Matter of Hofbauer*,[30] the New York Court of Appeals upheld the decision of parents to have a child with Hodgkin's disease treated with injections of laetrile and other nutritional and metabolic therapy, rather than with standard radiation treatment and chemotherapy.[31] The court emphasized that the parents had consulted with a physician about the use of laetrile therapy, other physicians were involved in the care of the child, the therapy appeared to be controlling the child's symptoms, and the parents had agreed to use standard therapy should the situation require it.[32]

By contrast, in *Matter of Sampson v. Taylor*,[33] a court ordered surgery for a child suffering from a severe facial disfigurement despite the parents' religious objections to the blood transfusions necessary for the surgery.[34] Although the disease did not pose an immediate threat to the life or the health of the child, the court found, based on expert testimony, that without the surgery the child would suffer serious and irreparable developmental and psychological problems.[35]

According to one New York trial court, once parents have authorized a course of treatment for their child, the child's refusal to consent to the treatment is generally irrelevant. In *Matter of Thomas B.*,[36] a fifteen-year-old boy who had a needle phobia refused to consent to a tumor biopsy that had been arranged by his mother.[37] The court ordered the biopsy to go

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exception despite the existence of statutes specifying the circumstances in which minors could consent to medical treatment. See *Belcher v. Charleston Area Med. Ctr.*, 188 W. Va. at 114–115, 422 S.E.2d at 836–837; *Cardwell v. Bechtol*, 724 S.W.2d at 743–745.

[27] See, e.g., *Matter of Hofbauer*, 47 N.Y.2d 648, 655, 419 N.Y.S.2d 936, 940 (1979); *Matter of Matthews*, 225 A.D.2d 142, 148–150, 650 N.Y.S.2d 373, 377–378 (App. Div. 1996); N.Y. Pub. Health Law § 2504(2) (McKinney 1999).

[28] See *Matter of Hofbauer*, 47 N.Y.2d at 655, 419 N.Y.S.2d at 941; *Matter of Matthews*, 225 A.D.2d at 148, 650 N.Y.S.2d at 377.

[29] *Matter of Hofbauer*, 47 N.Y.2d at 656, 419 N.Y.S.2d at 941.

[30] Ibid., 47 N.Y.2d at 655, 419 N.Y.S.2d at 940 (1979).

[31] Ibid., 47 N.Y.2d at 652, 656–657, 419 N.Y.S.2d at 938, 941.

[32] Ibid., 47 N.Y.2d at 656–657, 419 N.Y.S.2d at 941.

[33] *Matter of Sampson v. Taylor*, 65 Misc.2d 658, 317 N.Y.S.2d 641 (N.Y. Fam. Court Ulster Cty. 1970), *aff'd* 37 A.D.2d 668, 323 N.Y.S.2d 253 (App. Div. 1971), *aff'd*, 29 N.Y.2d 900, 328 N.Y.S.2d 686 (1972).

[34] Ibid., 65 Misc.2d at 675–676, 317 N.Y.S.2d at 658–659.

[35] Ibid., 65 Misc.2d at 660, 672, 675–676, 317 N.Y.S.2d at 644–645, 655, 658.

[36] 152 Misc.2d 96, 574 N.Y.S.2d 659 (Fam. Ct. Cattaraugus County 1991).

[37] Ibid., 152 Misc.2d at 97, 574 N.Y.S.2d at 660.

forward, stating that persons under eighteen years of age may not override their parents' consent to treatment.[38]

Utilizing the mature minor doctrine, however, the West Virginia Supreme Court has held that physicians may not perform medical procedures on or administer treatments to mature minors without their consent, even if their parents consent to the procedures or treatments.[39]

In the context of medical research, federal regulations generally require that researchers obtain a child's "assent" before including the child in a research study when an institutional review board determines that the children are capable of assent.[40] Assent is defined as "a child's affirmative agreement to participate in research."[41] A child's failure to object to participation in a research project, without an affirmative agreement to participate, does not constitute assent.[42]

## Benefits and Risks of Predictive Testing of Children and Adolescents

### Benefits of Testing Children and Adolescents

### `Testing for Late-Onset Disorders

For familial late-onset disorders, clinical surveillance and/or preventive measures may be available for asymptomatic individuals. In those cases where optimal effectiveness of these measures requires implementation during childhood or adolescence, genetic testing of children is generally recommended. One example is familial adenomatous polyposis

(FAP), a rare form of familial colon cancer.[43] FAP is caused by inheritance of a single dominant gene mutation, which results in formation of up to thousands of precancerous colon polyps and, eventually, cancer.[44] In affected families, a DNA-based genetic test can identify which children require colonoscopic monitoring and eventual removal of the colon to

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[38] *Matter of Thomas B.*, 152 Misc.2d at 98–99, 574 N.Y.S.2d at 661. See also *Alfonso v. Fernandez*, 195 A.D.2d at 50–51, 606 N.Y.S.2d at 262 (subject to statutory exceptions, it is generally "for parents to consent or withhold their consent to the rendition of health services for their children").

[39] See *Belcher v. Charleston Area Med. Ctr.*, 188 W. Va. at 116, 422 S.E.2d at 838.

[40] See 45 C.F.R. § 46.408(a) (1999).

[41] Ibid., § 46.402(b).

[42] Ibid.

[43] FAP accounts for approximately 1 percent of the 135,000 cases of colon cancer diagnosed annually in the United States. American Cancer Society, *Cancer Facts and Figures* (Atlanta: American Cancer Society, 1996), Publication No. 5008-96.

[44] T. D. Gelehrter, F. S. Collins, and D. Ginsburg, *Principles of Medical Genetics*, 2d ed. (Baltimore: Williams and Wilkins, 1998), 265. FAP is caused by inheritance of one mutated copy of a gene called APC (adenomatous polyposis coli). APC is a tumor suppressor gene. For discussion of tumor suppressor genes, see Chapter 1, page 19.

prevent almost certain colon cancer by age forty.[45] Genetic testing also benefits children identified not to carry the family mutation, who are spared regular, uncomfortable, and expensive colonoscopic exams.

There are other single-gene late-onset disorders for which early preventive measures may be effective. One example is neurofibromatosis, a disorder characterized by formation of benign tumors of the nervous system that can lead to deafness, blindness, and confinement to a wheelchair. Genetic testing to identify children affected by familial neurofibromatosis allows monitoring and earlier surgical treatment, generally during adolescence.[46]

For most complex late-onset disorders for which susceptibility testing is available, however, there generally are no established preventive treatments that can be applied during childhood or adolescence. Examples include genetic susceptibility testing for breast cancer[47] and late-onset Alzheimer disease.[48] Even in cases for which medical interventions may exist, decisions about whether to test children may still be difficult. Unconfirmed medical interventions pose medical risks, and for susceptibility testing that is not 100 percent predictive, a child who tests positive for a susceptibility variant will not necessarily develop the disease.[49]

Despite the absence of an established medical benefit, parents (or adolescents) still might seek genetic testing for their children (or themselves) to determine risks for familial late-onset disorders such as Huntington disease. They also may seek testing for late-onset disorders for which available interventions or surveillance measures are just as likely to be successful when initiated in adulthood, for example, breast cancer susceptibility testing. In these cases, testing may be requested to reduce uncertainty and/or to facilitate life-planning decisions.[50] For adolescents of reproductive age, these may include reproductive decisions for the near future.[51]

### *Carrier Testing for Recessive Disorders*

The purpose of carrier testing for recessive disorders such as cystic fibrosis, Tay-Sachs disease, and sickle cell disease is generally to guide marital and/or reproductive

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[45] For a description of the test, see Chapter 2, page 38. The gene is called APC (adenomatous polyposis coli).

[46] "Insurance and the New Genetics: Test Results May Threaten Patients' Coverage," Howard Hughes Medical Institute website: *http://www.hhmi.org/genmed/insure.htm*, visited July 15, 1998; see also D. H. Gutmann et al., "The Diagnostic Evaluation and Multidisciplinary Management of Neurofibromatosis 1 and Neurofibromatosis 2," *Journal of the American Medical Association* 278 (1997): 51.

[47] See Chapter 3, page 63.

[48] See Chapter 3, page 67.

[49] See D. E. Hoffmann and E. A. Wulfsberg, "Testing Children for Genetic Predispositions: Is It in Their Best Interest?" *Journal of Law, Medicine and Ethics* 23 (1995): 331, 334.

[50] J. H. Fanos, "Developmental Tasks of Childhood and Adolescence: Implications for Genetic Testing," *American Journal of Medical Genetics* 71 (1997): 22, 23.

[51] D. Wertz and R. Gregg, "Optimizing Genetics Services in a Social, Ethical, and Policy Context: Suggestions from Consumers and Providers in the New England Regional Genetics Group," *The Genetic Resource* 10, no. 2 (1996): 44.

decision-making.[52] Persons may seek carrier testing based on an increased risk due to family history of a recessive disorder or high prevalence of carriers for a particular recessive disorder in certain ethnic or racial groups.[53] Under circumstances in which an adolescent at increased risk for carrier status is contemplating marriage or reproduction in the near future, testing could help guide marital or reproductive decisions. For example, in some ultra-Orthodox Jewish communities, a carrier screening program, Dor Yeshorim, screens high school seniors for carrier status for Tay-Sachs disease and several other recessive disorders.[54]

This benefit generally would not be relevant for a minor who has not reached reproductive age or who is not contemplating reproduction in the immediate future. Some commentators state that this information also may be of only minimal value to sexually active teenagers, who would unlikely be influenced by genetic risk information.[55] Others claim that early knowledge of carrier status could help a child adapt to the consequences of being a carrier over time, rather than having the information presented at the age of majority.[56]

## Risks of Testing Children and Adolescents

### *Testing for Late-Onset Disorders*

When a child tests positive for a genetic susceptibility and no preventive interventions exist, the risks associated with genetic testing of adults for late-onset orders, discussed in Chapter 3 of this report, generally apply.[57] Possible risks include the following: use of unconfirmed clinical interventions that may be unnecessary and/or harmful; discrimination; psychological harms, including stigmatization; and perturbation of family relationships. Some commentators argue that these harms may be amplified when the person tested is a child because of the child's developing and potentially fragile self-identity and the special risks of misguided parental treatment.[58] These special vulnerabilities may be further exaggerated in families with a genetic disorder in which a child has experienced the serious illness or death of a parent or siblings.[59]

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[52] See Chapter 3, page 50.
[53] Ibid.
[54] L. Wingerson, *Unnatural Selection: The Promise and the Power of Human Gene Research* (New York: Bantam Books, 1997), 8–11. For further discussion of the program, see Chapter 5, page 121.
[55] See E. W. Clayton, "Genetic Testing in Children," *Journal of Medicine and Philosophy* 22 (1997): 233, 243; American College of Medical Genetics/American Society of Human Genetics, "ASHG/ACMG Report — Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents," *American Journal of Human Genetics* 57 (1995): 1233, 1236–1237.
[56] "Genetic Interest Group Statement on Genetic Testing of Children, United Kingdom," *The Gene Letter* (August 1997), website: *http://www.geneletter.org*, visited January 29, 1998.
[57] See Chapter 3, page 70.
[58] Wertz et al., "Who Decides?" 876.
[59] Fanos, "Developmental Tasks of Childhood," 26

For testing of children, concerns about discrimination center on the possibility that earlier confirmation of genetic risk may limit insurability and/or employment prospects of the child when he or she reaches adulthood. As one child neurologist who treats patients with neurofibromatosis stated, while confirmation of risk for familial neurofibromatosis before or during adolescence may be clinically beneficial, parents "also have to decide whether they want their child to risk losing health insurance as soon as they turn eighteen."[60]

Another potential harm of testing children is that a positive test result may interfere with children's developing self-perception and their ability to integrate with their peer group. Some suggest that children with genetic disorders may lose self-esteem during a critical period for the development of self-identity,[61] although others claim that there is little evidence to support this fear.[62] Some express concerns that children have a limited understanding of the concept of illness, and as a result may blame themselves for their genetic susceptibility.[63]

Testing children, as in testing newborns,[64] also may perturb family relationships. Some commentators warn that parents who seek testing to reduce their own anxiety often are not prepared for the implications of a positive test result.[65] Parents may react inappropriately to a child's confirmed genetic susceptibility by overprotection, overindulgence, rejection, or inappropriate and possibly harmful preventive measures.[66] Some commentators state that testing of children for the common reason of "planning for the future" may become "restricting the future."[67] For example, testing may influence parental allocation of family resources. One commentator cites a case in which a mother requested testing of her two children who were at risk for Huntington disease "because she only had enough money to send one of them to Harvard."[68] Alternatively, parents may spend more resources on the affected child than they spend on unaffected siblings to "make up" for passing on the inherited disorder.[69] Even if a child tests negative for a familial mutation, he or she may experience problems of "survivor guilt" for escaping the genetic risk of a parent and/or siblings.[70]

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[60] "Insurance and the New Genetics" (quoting Dr. Mia McCollin, Massachusetts General Hospital). Potential for the adverse use of genetic information in insurance coverage decisions varies by state laws and other factors. For a discussion of genetic testing and insurance, see Chapter 9.

[61] See Wertz et al., "Who Decides?" 876; Fanos, "Developmental Tasks of Childhood," 23–24; American College of Medical Genetics/American Society of Human Genetics, "ASHG/ACMG Report," 1236.

[62] C. B. Cohen, "Wresting with the Future: Should We Test Children for Adult-Onset Genetic Conditions?" *Kennedy Institute of Ethics Journal* 8 (1998): 111, 114.

[63] See Wertz et al., "Who Decides?" 876.

[64] See Chapter 6, page 162.

[65] D. C. Wertz, J. H. Fanos, and P. Reilly, "Testing Children and Adolescents: Recommendations for Avoiding Harm," *The Genetic Resource* 8, no. 2 (1994): 16, 17.

[66] Ibid.; Fanos, "Developmental Tasks of Childhood," 24; American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1236.

[67] Wertz et al., "Recommendations for Avoiding Harm," 17.

[68] M. Murray, "Nancy Wexler," *New York Times Magazine*, February 13, 1994, 28, 31 (quoting Dr. Nancy Wexler, New York State Psychiatric Institute).

[69] J. Holland, "Should Parents Be Permitted to Authorize Genetic Testing for Their Children?" *Family Law Quarterly* 321 (1997): 321, 340.

[70] Fanos, "Developmental Tasks of Childhood," 26.

### *Carrier Testing for Recessive Disorders*

When an individual tests positive as a carrier for a recessive disorder, a principal risk is that the person may not understand that carriers are generally healthy and unaffected by disease. Some claim that these risks may be greater when parents request testing of their children because children may be more emotionally vulnerable and/or more likely to misunderstand test results.[71] This may be especially true in children who have a family history of a particular disorder.[72] There also is a risk that parents may misunderstand the information and accord "undue emotional significance" to carrier status or inaccurately relay test results to a child at the time of testing or later.[73] Another commentator cites a risk that the child's right of privacy in future marital and reproductive decisions may be compromised by parental knowledge of carrier status.[74] Risks of stigmatization and discrimination also exist.[75]

## Weighing the Benefits and Risks: The Roles of Parents, Children, and Providers

### Parental Decisions to Test Children and Adolescents

Most policy and professional genetics groups agree that testing of children is appropriate when established clinical interventions exist and that, in all testing decisions, the best interests of the child should be primary.[76] In the absence of a clear medical benefit to the child, most commentators opine that avoidance of potential testing-associated harms and preservation of the minor's future autonomy should be

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[71] Ibid.; Clayton, "Genetic Testing in Children," 243.

[72] J. H. Fanos, "My Crooked Vision: The Well Sib Views Ataxia Telangiectasia," *American Journal of Medical Genetics* 87 (1999): 420; Fanos, "Developmental Tasks of Childhood," 23.

[73] Fanos, "Developmental Tasks of Childhood," 25. For a discussion of parental misunderstanding of carrier status, see Chapter 6, page 162.

[74] D. S. Davis, "Discovery of Children's Carrier Status for Recessive Genetic Disease: Some Ethical Issues," *Genetic Testing* 2 (1998): 323.

[75] For a discussion of carrier testing and discrimination risks, see Chapter 5, page 115.

[76] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 10; National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of Health, 1997), 13; World Health Organization, Human Genetics Programme, "Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetics Services," Report of a WHO Meeting on Ethical Issues in Medical Genetics (Geneva, December 16–17, 1997); American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1233; American Medical Association Council on Ethical and Judicial Affairs, Opinion 2.138, "Genetic Testing of Children," *Code of Medical Ethics; Current Opinions*, 1998–1999 ed. (Chicago: American Medical Association).

the overriding considerations.[77] For example, the Institute of Medicine Committee on Assessing Genetic Risks (IOM Committee) states that children "should generally be tested only for genetic disorders for which there exists an effective curative or preventive treatment that must be instituted early in life to achieve maximum benefit."[78] The American Society of Human Genetics (ASHG) and the American College of Medical Genetics (ACMG) state that "timely medical benefit to the child should be the primary justification for genetic testing in children and adolescents."[79]

### *Testing for Late-Onset Disorders*

Some genetics providers, professional guidelines, and testing laboratories refuse to test or strongly recommend against testing of minors for genetic predisposition to particular late-onset disorders, including Huntington disease[80] and breast cancer.[81] Other commentators, however, maintain that such blanket statements overemphasize the potential harms of testing and fail to acknowledge legitimate interests and obligations of parents, who, they claim, are generally in the best position to determine the child's best interests.[82] They state that preservation of a child's future decision-making autonomy should not be the only relevant factor and suggest that testing may, in fact, expand a child's future options.[83] One commentator states that no substantial harms to tested children have been proven and that testing may pose significant benefits to children and their families.[84]

Both the American Medical Association Council for Ethical and Judicial Affairs (AMA Council) and the ASHG/ACMG guidelines generally oppose parental requests for predictive genetic testing of children in the absence of a medical

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[77] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 10; American Medical Association Council, "Genetic Testing of Children"; American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1233; NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 13; Working Party of the Clinical Genetics Society (UK), "The Genetic Testing of Children," *Journal of Medical Genetics* 31 (1994): 785; Wertz and Gregg, "Suggestions from Consumers and Providers," 45; World Health Organization, "Proposed International Guidelines."

[78] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 10.

[79] American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1233.

[80] L. Went, "Ethical Policy Issues Policy Statement on Huntington's Disease Molecular Genetics Predictive Test," *Journal of Medical Genetics* 27 (1990): 34; M. Block and M. R. Hayden, "Predictive Testing for Huntington Disease in Childhood: Challenges and Implications," *American Journal of Human Genetics* 46 (1990): 1; Wertz and Reilly, "Laboratory Practices," 1164–1165.

[81] B. B. Biesecker et al., "Genetic Counseling for Families with Inherited Susceptibility to Breast and Ovarian Cancer," *Journal of the American Medical Association* 269 (1993): 1970, 1973.

[82] Cohen, "Wresting with the Future," 111; M. Z. Pelias and S. H. Planton, "Genetic Testing in Children and Adolescents: Parental Authority, the Rights of Children, and Duties of Geneticists," in *Genetics and the Law: The Ethical, Legal, and Social Implications of Genetic Technology and Biomedical Ethics* (Chicago: University of Chicago Law School Roundtable, 1996).

[83] Cohen, "Wrestling with the Future," 117.

[84] Ibid., 112.

benefit, yet both also acknowledge that testing decisions can be complex.[85] The AMA Council maintains that parental decisions to test children should be respected as long as they reflect a reasonable balance of advantages and disadvantages. The ASHG/ACMG guidelines state that, in some cases, the balance of risks and benefits may favor testing.[86]

One circumstance in which some commentators think that parental requests for predictive genetic testing may merit special consideration, even in the absence of preventive or therapeutic measures, is when the familial disorder tested for manifests at some time during childhood, such as X-linked muscular dystrophy. There are two forms of this disorder, resulting from different mutations in the same gene. Duchenne muscular dystrophy generally manifests at age three to five; Becker muscular dystrophy is a milder and more variable form that manifests later in childhood or adolescence.[87] The AMA Council maintains that, when a child is at risk for a condition with pediatric onset for which preventive or other therapeutic measures are not available, "parents generally should have discretion to decide about genetic testing."[88] Other commentators, agreeing with this recommendation, note that anxiety created by "every stumble or expression of fatigue" in a boy potentially at risk for Duchenne muscular dystrophy may overshadow his life.[89] The IOM Committee, by contrast, concluded that predictive genetic testing of children is not appropriate for untreatable disorders, even when symptoms of the disorder may manifest during childhood.[90]

***Carrier Testing for Recessive Disorders***

Most commentators agree that, in general, parents should not request carrier testing for their children and that testing should be deferred until children reach maturity.[91] Some commentators note that parental decisions for carrier

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[85] American Medical Association Council, "Genetic Testing of Children"; American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1238.

[86] American Medical Association Council, "Genetic Testing of Children"; American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1233, 1238. Case-by-case variables include disease penetrance, disease severity, age of disease onset (e.g., childhood versus midlife), maturity of the child, and family dynamics.

[87] M. W. Thompson, R. R. McInnes, and H. F. Willard, *Genetics in Medicine,* 5th ed. (Philadelphia: W. B. Saunders Company, 1986), 289–290. Boys affected by Duchenne muscular dystrophy generally die by age twenty. The disorder is classified as the Becker form if the affected child is still walking by age sixteen.

[88] American Medical Association Council, "Genetic Testing of Children."

[89] Harper and Clarke, "Should We Test Children?" 1206.

[90] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 10.

[91] American Medical Association Council, "Genetic Testing of Children"; American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1233; Wertz and Gregg,

testing may be justified in exceptional situations, such as development of an intimate relationship between two young adolescents, both of whom have family members with cystic fibrosis.[92] One group, however, supports broader parental control in this area, stating that, with adequate counseling, parents have the right to make an informed choice about testing the carrier status of their children.[93]

## Participation of Minors in Testing Decisions

### *Role of Minor's Assent or Consent*

For predictive genetic testing requests for children, the ASHG/ACMG guidelines call on providers to counsel parents and the child, commensurate with the child's maturity, to help them assess benefits and risks and to act in the perceived best interests of the child. The guidelines recognize that, although the legal age for medical decision-making is generally eighteen, studies have found that the ability of children to make decisions develops as they mature.[94] Acknowledging the successive stages of cognitive and moral development of children, the guidelines call on parents and providers to be attentive to a child's increasing interest and ability to participate in decisions in his or her own welfare.[95] They recommend that, in general, providers should obtain assent from children who are age seven or older and consent from adolescents.[96] A child's assent to testing is the child's "affirmative agreement" to participate in testing and "only requires a rudimentary understanding of risk and benefit."[97]

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"Suggestions from Consumers and Providers," 44; Clayton, "Genetic Testing in Children," 244; Davis, "Discovery of Children's Carrier Status," 325.

[92] Davis, "Discovery of Children's Carrier Status," 323; Wertz, Fanos, and Reilly, "Who Decides?" 875.

[93] "Genetic Interest Group Statement on Genetic Testing of Children."

[94] American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1238. See R. F. Weir and J. R. Horton, "Genetic Research, Adolescents, and Informed Consent," *Theoretical Medicine* 16 (1995): 347, 353–355.

[95] American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1233–1234, 1238. They note that children mature at different rates but state that, generally, children obtain sufficient cognitive skills to provide assent by age seven.

[96] Ibid. The American Academy of Pediatrics emphasizes that adolescents who are fourteen or older are the most likely to have developed the decisional skills necessary to enable them to make informed decisions about their medical care. American Academy of Pediatrics, "Informed Consent, Parental Permission, and Assent in Pediatric Practice," *Pediatrics* 95 (1995): 314, 317. See Weir and Horton, "Genetic Research, Adolescents and Informed Consent," 353–355.

[97] American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1238; Wertz, Fanos, and Reilly, "Genetic Testing for Children and Adolescents," 877. The American Academy of Pediatrics maintains that physicians should obtain assent to medical treatments from older children and, in most cases, informed consent to medical treatments from adolescents and young adults. The Academy contends that assent should include the following elements "1. Helping the patient achieve developmentally appropriate awareness of his or her condition. 2. Telling the patient what he or she can expect with the tests and treatment(s). 3. Making a clinical assessment of the patient's understanding of the situation and the factors influencing how he or she is responding (including whether there is inappropriate pressure to accept testing or therapy). 4. Soliciting an expression of the patient's willingness to accept the proposed care." American Academy of Pediatrics, "Informed Consent, Parental Permission, and Assent in Pediatric Practice," 315. Although the Academy recognizes that there are circumstances in which children will be given medical care despite their refusal to assent, it asserts that in those circumstances, children

When the balance of risks and benefits of testing is uncertain, the ASHG/ACMG guidelines state that providers should respect the decisions of competent adolescents and their families; when potential harms clearly outweigh potential benefits, providers should discourage testing. In cases where parents request testing but the minor does not, some commentators state that the provider should act as an advocate for the minor.[98] Both the ASHG/ACMG guidelines and the AMA Council assert that a provider has no obligation to provide a medical service that is not in the best interests of the child.[99] Other commentators agree, noting that physicians have greater room for overriding parental choices made on the behalf of children than they do for overriding choices made by adults for themselves.[100]

### *Adolescent-Initiated Requests for Testing*

In some cases, adolescents may be the primary requestors of predictive testing, with or without parental support. They may do so to make life-planning decisions, including reproductive decisions for the near future.[101] For Huntington disease predictive testing, one study in Great Britain concluded that requests for testing initiated by minors were rare but did occur. The study estimated that 1.9 percent of requests for genetic testing for Huntington disease were from persons age twenty or younger.[102]

Another group, the 1997 National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing acknowledged that legal adulthood "is a somewhat arbitrary concept" and that in families with a considerable disease burden, older teenagers might request testing for themselves.[103] They called for more research in this area but recommend that testing of minors for perceived psychosocial benefits should be avoided. Others state that genetic testing for late-onset disorders may be useful to minors of reproductive age and that, in such cases, the minor should be the primary decision-maker.[104] The ASHG/ACMG guidelines state that "substantial psychosocial benefits to the competent adolescent" may justify genetic testing.[105] The guidelines maintain that as adolescents' decision-making capacity increases, additional

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should be told that their refusal to assent will not stop the treatments from going forward. The Academy emphasizes that no one should ask for a child's assent without intending to "weigh seriously" the child's decision. Ibid., 315–316.

[98] Wertz, Fanos, and Reilly, "Who Decides?" 880.

[99] American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1233, 1234.

[100] Clayton, "Genetic Testing in Children," 234; Wertz et al., "Who Decides?" 878.

[101] Wertz and Gregg, "Suggestions from Consumers and Providers," 44.

[102] J. Binedell et al., "Huntington's Disease Predictive Testing: The Case for an Assessment Approach to Requests from Adolescents," *Journal of Medical Genetics* 33 (1996): 912, 918. In data from other European Community testing centers, the authors state that five out of thirty-nine applicants under age eighteen were self-referrals, as opposed to requests made by parents or professionals. Ibid., 912.

[103] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 13.

[104] Wertz, Fanos, and Reilly, "Who Decides?" 880; Wertz and Gregg, "Suggestions from Consumers and Providers," 44.

[105] American Society of Human Genetics/American College of Medical Genetics, "ASHG/ACMG Report," 1238.

consideration should be given to their wishes, "even when those wishes differ from those of their parents or when those wishes are not clearly in the child's best interest."[106] They stipulate that the adolescent should meet conditions of competence, voluntariness, and adequate understanding of information,[107] and they suggest that other consultations, for example, with psychologists and/or ethics boards, might be appropriate.[108] Other commentators advocate assessment of an adolescent who requests testing by an expert child/adolescent clinical psychologist or psychiatrist.[109]

## Genetic Information and Adoption

### Disclosure of Adoptees' Genetic Information to Prospective Adoptive Parents

For most of this century, adoption agencies disclosed little medical information about prospective adoptive children and their biological families to prospective adoptive parents.[110] In the last twenty years, adoption professionals have come to support full disclosure of medical information to prospective adoptive parents to facilitate proper health care for adopted children and to ensure that children with special health needs are placed with families who are emotionally and financially capable of dealing with those needs.[111]

New York and other states currently require adoption agencies to disclose to prospective adoptive parents the medical histories of prospective adoptees and their biological parents.[112] New York specifically mandates that the medical histories include "all available information setting forth conditions or diseases believed to be hereditary."[113] Agencies that fail to disclose such information are subject to lawsuits for wrongful adoption.[114] However, because adoption agencies are not involved in private placement adoptions (i.e., adoptions where the natural parent retains custody of the child until the order of adoption is signed),[115] the disclosure requirement does not apply to such adoptions.[116]

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[106] Ibid.
[107] Ibid., 1233.
[108] Ibid.
[109] Binedell et al., "Huntington's Disease Predictive Testing," 916.
[110] See M. B. Blair, "The Uniform Adoption Act's Health Disclosure Provisions: A Model That Should Not Be Overlooked," *Family Law Quarterly* 30 (1996): 427, 428.
[111] See ibid., 432–433.
[112] M. J. Blank, "Adoption Nightmares Prompt Judicial Recognition of the Tort of Wrongful Adoption: Will New York Follow Suit?" C*ardozo Law Review* 15 (1994): 1687, 1725–1728; N.Y. Soc. Serv. Law § 373-a (McKinney 1999); 18 N.Y.C.R.R. § 357.3(b) (1998); D. M. B. Blair, "Lifting the Genealogical Veil: A Blueprint for Legislative Reform of the Disclosure of Health Related Information in Adoption," *North Carolina Law Review* 70 (1992): 681, 713–714, 732–736.
[113] N.Y. Soc. Serv. Law § 373-a (McKinney 1999); 18 N.Y.C.R.R. § 357.3(b)(7) (1998).
[114] See, e.g., *Juman v. Louise Wise Servs.*, 211 A.D.2d 446, 620 N.Y.S.2d 371 (N.Y. App. Div. 1995); M. Freundlich and L. Peterson, *Wrongful Adoption: Law, Policy, & Practice* (Washington, D.C.: Child Welfare League of America, 1998), 11–26.
[115] See M. Waldman, "Adoption," 2 Am. Jur.2d § 6 (1999).
[116] See Blair, "Lifting the Genealogical Veil," 718–720; N.Y. Soc. Serv. Law § 373-a (McKinney 1999) (requiring adoption agencies to disclose the medical histories of prospective adoptees and their biological parent to prospective adoptive parents, but not mentioning disclosure of such information in private placement adoptions).

Like many other states, New York does not require adoption agencies to make any affirmative effort to uncover the medical histories of prospective adoptees and their biological parents, but simply mandates that the agencies disclose them "to the extent they are available."[117] Some commentators have argued that the law should require adoption agencies and licensed professionals involved in private placement adoptions to use "reasonable efforts" to obtain medical histories of prospective adoptees, their parents, and their extended families and to disclose them to the prospective adoptive parents.[118] Some states have imposed such a duty.[119] One commentator maintains that persons who collect this information should receive specialized training.[120]

While advocating that adoption agencies should collect all "material" medical information about prospective adoptees and disclose that information to prospective adoptive parents,[121] some commentators have raised questions about the imposition of a legal duty to collect and disclose such information.[122] In general, they are concerned about the amount of investigation and disclosure that would be required to satisfy such a duty. For example, they question whether adoption agencies would be required to contact anyone in the child's family besides the child's biological parents or to conduct medical inquiries even over the objections of the child's biological parents. Some commentators have expressed concern that conducting medical inquiries over the objections of biological parents might discourage others from relinquishing their children for adoption.[123]

The ASHG contends that obtaining adoptees' genetic histories should be part of the standard adoption process and that the histories should be placed in the prospective adoptees' medical files.[124] They also maintain that, when medically appropriate, an adoptee's genetic

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[117] N.Y. Soc. Serv. Law § 373-a (McKinney 1999); 18 N.Y.C.R.R. § 357.3(b) (1999); Blank, "Adoption Nightmares," 1725–1726.

[118] See National Conference of Commissioners on Uniform State Laws, *Uniform Adoption Act* §§ 2-106, 7-105, & commentary (1994); Blair, "The Uniform Adoption Act's Health Disclosure Provisions," 443–444; Blair, "Lifting the Genealogical Veil," 736–737, 745; Freundlich and Peterson, *Wrongful Adoption*, 39, 60–65. For a description of what "reasonable efforts" to obtain medical history information might include, see Blair, "The Uniform Adoption Act's Health Disclosure Provisions," 447–452.

[119] See, e.g., *McKinney v. State*, 134 Wash.2d 388, 394–396, 950 P.2d 461, 465 (1998); Wash. Rev. Code Ann. § 26.33.350(4) (West 1999); D. M. B. Blair, "The New Oklahoma Adoption Code: A Quest to Accommodate Diverse Interests," *Tulsa Law Review* 33 (1997): 177, 265; Okla. Stat. tit. 10 § 7504-1.2(D) (1998); Mich. Comp. Laws Ann. § 710.27(1), (2) (West 1999).

[120] Blair, "The Uniform Adoption Act's Health Disclosure Provisions," 443; Blair, "Lifting the Genealogical Veil," 743–744, 763.

[121] Freundlich and Peterson, *Wrongful Adoption*, 60–65. These commentators define "material information" as "information that may be important to prospective adoptive parent in deciding whether to adopt a particular child." Ibid., 60.

[122] Ibid., 39–42.

[123] Ibid., 40–42.

[124] American Society of Human Genetics Social Issues Committee, "Report on Genetics and Adoption: Points to Consider," *American Journal of Human Genetics* 48 (1991): 1009.

information should be shared with the adoptee's biological and adoptive parents.[125] Asserting that the process of obtaining genetic information about prospective adoptees should respect the parties' right of privacy, the ASHG also contends that parties should have

the right not to participate, or to cease participating, in the collection of genetic information on behalf of the adoptee.[126]

**Genetic Testing of Prospective Adoptees**

Some adoption professionals advocate that prospective adoptive children undergo thorough medical examinations prior to being adopted and that the results of those examinations should be disclosed to prospective adoptive parents.[127] Doing so, these commentators contend, would help ensure that children are placed with families that are emotionally and financially able to deal with health conditions they may have and that will obtain proper medical care from their adoptive parents.[128] Currently, New York does not require adoption agencies or persons involved in private placement adoptions to perform medical examinations on prospective adoptive children prior to adoption.[129]

Although requests for genetic testing of prospective adoptees appear to be relatively rare,[130] they do occur. One source reported receiving requests from adoption agencies to perform Huntington disease testing of newborns who were at 50 percent risk for having the genetic mutation that causes the disease.[131] Recently, an adoption agency requested Johns Hopkins University to perform Huntington disease testing on a fetus because the mother who planned to put the baby up for adoption had relatives who had died of the disease.[132] As the number and availability of genetic tests increases, the number of requests for genetic testing of prospective adoptees may grow.

Commentators stress that the best interests of the prospective adoptees should be the guiding principle in determining whether they should undergo genetic testing.[133] Some commentators contend that prospective adoptees should undergo genetic testing only in

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[125] Ibid.
[126] Ibid.
[127] Freundlich and Peterson, *Wrongful Adoption*, 64–65; Blair, "Lifting the Genealogical Veil," 758–760; American Academy of Pediatrics, "Initial Medical Evaluation of an Adopted Child," *Pediatrics* 88 (1991): 642.
[128] See Blair, "Lifting the Genealogical Veil," 758.
[129] See Blank, "Adoption Nightmares," 1726.
[130] Telephone interview with Madelyn D. Freundlich, Esq., Executive Director, The Evan B. Donaldson Adoption Institute, New York, NY, May 10, 1999; telephone interview with Katherine Legg, Executive Director, Spence Chapin Adoption Agency, New York, NY, May 5, 1999; telephone interview with Aaron Britvan, Esq., Chair of the New York State Bar Association Committee on Adoption, New York, NY, May 4, 1999.
[131] M. Morris, A. Tyler, and P. S. Harper, "Adoption and Genetic Prediction for Huntington's Disease," *The Lancet* ii (1988): 1069, 1069.
[132] L. Neergaard, "Accuracy for Gene Tests Unregulated," *The Associated Press,* AP Online, September 20, 1999.
[133] American Society of Human Genetics and American Society of Medical Genetics, "ASHG/ACMG Statement Genetic Testing in Adoption," *American Journal of Human Genetics* 66 (2000): 761, 762*;* Clinical Genetics Society, "The Genetic Testing of Children," *Journal of Medical Genetics* 31 (1994): 785, 790; Morris, Tyler, and Harper, "Adoption and Genetic Prediction," 1069.

situations where it would be appropriate to test other children.[134] Most commentators agree that it is generally inappropriate to perform genetic tests on prospective adoptees that detect reproductive risks or predispositions to late-onset disorders for which preventive measures are not currently available.[135] Some of these commentators are concerned that such testing treats prospective adoptees as commodities.[136] At Johns Hopkins University, practitioners refused to perform Huntington disease testing on the fetus discussed above because they felt that it was unfair to jeopardize the prospective child's chances for adoption by testing it for a disease that would not occur until middle age and for which a cure might be developed by that time.[137]

One issue that has only recently been addressed by commentators is whether it is ever appropriate to perform genetic testing on prospective adoptees for untreatable childhood-onset conditions such as Duchenne muscular dystrophy. The ASHG and the ACMG contend that such testing is appropriate "when there is some health-related indication of the need to test," such as "symptoms and family history."[138] Outside of the adoption context, commentators disagree about whether it is appropriate to have children undergo such testing.[139]

## Conclusions and Recommendations

### Predictive Genetic Testing to Determine Adult-Onset Disease and Reproductive Risks

**The best interests of the child, including respect for the child's future autonomy, should be the primary consideration in decisions about predictive genetic testing of children. Predictive genetic testing of children is clearly appropriate when test results will provide information relevant to current decisions about the child's care, such as decisions to institute prophylactic treatment. Where the benefits to the child are less clear, however, predictive genetic testing should be approached with caution, given that testing can also lead to significant harms.**

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[134] M. D. Freundlich, "The Case against Preadoption Genetic Testing," *Child Welfare* 77 (1998): 663, 671–672; American Medical Association Council, "Genetic Testing of Children"; Wertz, Fanos, and Reilly, "Who Decides?" 875, 880.

[135] See American Society of Human Genetics and American Society of Medical Genetics, "Genetic Testing in Adoption," 763–764; Wertz, Fanos, and Reilly, "Who Decides?" 880; Morris, Tyler, and Harper, "Adoption and Genetic Prediction," 1069.

[136] Wertz, Fanos, and Reilly, "Genetic Testing of Children and Adolescents," 880; Freundlich, "The Case against Preadoptive Genetic Testing," 672.

[137] The Associated Press, "Accuracy for Genetic Tests Unregulated," September 20, 1999, *New York Times* website, *http://www.nytimes.com/aponline/w/AP-Genetic-Testing.html*, visited October 1, 1999.

[138] American Society of Human Genetics and American Society of Medical Genetics, "Genetic Testing in Adoption," 763.

[139] See page 227, this chapter.

The current standard of care, as reflected in statements by numerous professional societies, generally discourages predictive genetic testing of children for adult-onset diseases or to determine a child's future reproductive risks in the absence of a medical benefit. We agree with this standard and believe that, generally, such testing should be delayed until the child reaches the age of majority and can make his or her own testing decisions. Children should be free, upon adulthood, to make their own choices about predictive testing for late-onset diseases; as experience in the general population shows, many of these children, when they reach the age of majority, will choose not to undergo genetic testing for late-onset disorders, particularly for conditions for which effective preventive or therapeutic interventions do not exist.

While parents may wish to reduce anxiety about their child's future, testing often will confirm, rather than allay, risk. This may increase parental anxiety and also pose psychological, developmental, and even medical harms to the child. Parental knowledge of a child's future health also might inappropriately restrict a child's future, intentionally or otherwise. Children may be especially vulnerable to psychological harm, especially if they have witnessed affected family members suffer from the disease for which they are at risk. Testing also could cause physical harm to a child if an unconfirmed prophylactic intervention is used. Knowledge about safety and effectiveness of medical interventions generally will increase over time; thus, medical and psychological harms might be avoided by later, versus earlier, testing. For genetic susceptibility tests that are not 100 percent predictive, the understanding of a test's clinical predictive value also is likely to improve with time, and earlier testing may cause unwarranted anxiety.

Parents' desire to learn genetic information for purposes of their own future reproductive planning does not justify testing children for late-onset or reproductive interests. The better approach in such situations is for the parents to undergo carrier screening prior to initiating another pregnancy.

### Predictive Genetic Testing to Determine Risks for Pediatric-Onset Disease

**When a healthy child is at risk for a pediatric-onset disorder, predictive genetic testing to confirm or allay disease risks may be in the best interests of the child, even if preventive or therapeutic interventions are not available.**

When a child is at risk for a serious genetic disorder that can become symptomatic during childhood or adolescence, for example, cystic fibrosis or muscular dystrophy, preservation of the child's future right to make a testing decision is not relevant. The occurrence of a pediatric-onset disorder, unlike an adult-onset disorder, also will directly affect parental responsibilities. In such cases, we believe that exceptions to the recommendation that testing of children be discouraged are justified. Predictive testing for a child may help the family prepare for its future medical and other needs. Testing also may diminish the anxiety associated with interpreting their child's potential early symptoms of disease.

## The Role of Health Care Providers in Guiding Predictive Genetic Testing Decisions

**Health care providers play a critical role in guiding decisions about predictive genetic testing of children. When faced with a parent's request for predictive genetic testing of a healthy child or with a request initiated by a healthy adolescent, providers should counsel the parents and the child, commensurate with the child's maturity, and help families balance potential benefits and risks of testing. When the balance of potential risks and benefits is uncertain, providers should generally respect the decisions of parents.**

Determination of the balance of potential benefits and risks of predictive genetic testing will often be complex, based on personal and familial factors and also on evolving data about a test's predictive power and the benefits of new medical interventions. This complexity underscores the need for active involvement of health care providers in guiding a family's testing decision. It is critical that parents and older children receive appropriate counseling and education about the power and limitations of testing, as well as its possible benefits and risks. Providers have an important role in helping families reach a decision that is in the child's and the family's best interests.

In some cases, the balance of benefits and risks may be uncertain. Often, parental requests for testing will be for children who are not old enough to be involved in the counseling and decision-making process. We agree with professional groups that hold that, in such cases, providers should respect the wishes of parents. We further agree that parental responsibilities often include decisions that open some paths while closing others for a child and that parents are generally in the best position to decide what is in their child's best interests.

## Conflicts between Parents and Adolescents

**Ideally, predictive genetic testing of children will be performed with both the consent of the parents and either the assent or consent of the child, depending on the child's maturity. The Task Force members hold differing views about cases where parents and adolescents disagree about genetic testing decisions. Where the balance of benefits and risks is uncertain, some members believe that providers should generally defer to the wishes of the parent, even over the objection of a mature adolescent. Others would defer to the**

**adolescent's decision in at least some cases, particularly when an adolescent opposes testing.**

Testing that proceeds with the informed consent of the parents and the consent or assent of their minor children is the ideal. The process of counseling and consent (or assent) of the involved family members will likely benefit the family and help them understand and accept test results. The process also may identify situations in which parents or children are clearly unprepared for testing.

Conflicts, however, may arise. Parents may request testing of a child or adolescent who opposes testing. Clearly, when there is a confirmed medical benefit to testing, as in the case of testing to determine risk for the familial colon cancer FAP,[140] parental decisions to test should be determinative. When no confirmed benefit exists, the appropriate action may be less clear. Most Task Force members agree that, when the balance of benefits and risks is uncertain, parents should have the final decision. However, when potential harms to the child clearly outweigh the benefits of testing, the Task Force agrees with others that the physician's first responsibility is to the health of the child or adolescent.

In some cases, adolescents who do not meet the definition of an emancipated minor[141] may initiate a request for predictive testing. Providers must assure that the adolescent's request is mature and that he or she understands the potential harms associated with testing. They also should counsel parents and seek their consent. Although we acknowledge the ability of some older adolescents to make mature decisions, the majority of Task Force members think that adolescents who are dependent on their parents and who do not have parental consent for testing should wait until they reach the age of majority.

**Disclosure of Test Results to Minors**

**If a child or adolescent has provided assent or consent for predictive genetic testing, he or she also should be informed of test results and their meaning, commensurate with his or her maturity and with his or her desire to have this information.**

Parents sometimes request that test results not be disclosed to the child or adolescent tested. Ideally, disclosure issues should be addressed during pretest counseling. When conflicts about disclosure arise, we agree with professional societies and others that state that when a child or adolescent of sufficient maturity has provided assent or consent and requests genetic test results, that request should be respected by parents and given priority by providers over parents' requests to conceal the results. When younger children are involved, providers should work with families to promote disclosure at the appropriate point in the child's development. When children who are

[140] See page 222, this chapter.
[141] See page 218, this chapter.

unaware that they have been tested reach adulthood, providers should inform them that testing was performed, provide or arrange for appropriate counseling, and offer them the option of learning the test results.

### Genetic Testing of Prospective Adoptees by Their Current Caregivers

**Caregivers of prospective adoptive children should ensure that the children undergo genetic testing when such testing is necessary for the children's current health care.**

Caregivers of prospective adoptive children, such as foster parents, have an obligation to provide for the children's current health care needs. These needs can sometimes include diagnostic genetic testing. For example, when medically indicated, custodians should ensure that children undergo predictive genetic tests for conditions for which treatments or preventive measures should begin immediately, for example, FAP testing of older children.[142]

### Genetic Testing of Prospective Adoptees at the Request of Prospective Adoptive Parents

**Genetic testing should be performed on a prospective adoptee at the request of prospective adoptive parents only when (1) the testing is medically indicated and can reveal that a child is highly likely to develop extraordinary health care needs during childhood, (2) the testing will help ensure that the child is placed with a family who is capable of dealing with those needs, and (3) the prospective parents are otherwise committed to adopting the child.**

Adoption professionals have come to recognize that full disclosure of a prospective adoptee's medical history to prospective adoptive parents is necessary to facilitate proper health care for adopted children and to ensure that children with special health needs are placed with families who are emotionally and financially capable of dealing with those needs.[143] Similarly, to the extent possible, prospective adoptees should not be placed with families who will be unable to cope with children who are likely to have serious health conditions during childhood that have a strong genetic basis, such as Duchenne muscular dystrophy.[144]

In some circumstances, genetic testing may help identify children who, although currently asymptomatic, are likely to develop special health care needs during childhood.

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[142] See page 221–222, this chapter. See also Chapter 3, page 68.
[143] See page 230, this chapter.
[144] Ibid.

If genetic testing is medically indicated and can reveal that a child is highly likely to develop extraordinary health care needs during childhood, it may be appropriate for prospective adoptive parents to request such testing prior to finalizing an adoption. In all cases, the purpose of such testing should be to help ensure that the child is placed with parents capable of dealing with the child's special needs.

We recognize that testing prospective adoptees at the request of prospective adoptive parents risks treating the children as commodities. Accordingly, such testing should be approached with caution and should be performed only for serious, highly penetrant genetic disorders and only after the parents are otherwise committed to adopting the child.

Under this standard, it would generally be inappropriate to perform genetic testing of prospective adoptees to determine risk for adult-onset disease or to assess reproductive risks.

**Collection and Disclosure of Prospective Adoptees' Medical Histories**

**New York law should be amended to require that parties placing a child for adoption make reasonable efforts to collect a complete medical and genetic history of the child and provide it to the prospective adoptive parents. New York law also should be amended to require the parties to make reasonable efforts to collect the medical and genetic histories of the birth parents and close blood relatives of the prospective adoptee and disclose them to the prospective adoptive parents. The parties should collect and disclose this information in a manner that respects the privacy of the persons from whom it is obtained and the subjects of the information. For example, the medical and genetic histories of the prospective adoptees' relatives should be disclosed to prospective adoptive parents with all identifying information removed.**

The collection of the medical and genetic history of prospective adopted children and their close relatives may be crucial for the children's health care. Currently, New York law does not require adoption agencies or other parties placing a child for adoption to make any affirmative efforts to uncover the medical histories of prospective adoptees. New York law should be amended to mandate that such reasonable efforts be made.

Although New York law currently requires disclosure only of the medical histories of prospective adoptees and their biological parents, the medical histories of close relatives are also relevant to the children's health care. We therefore recommend that New York law be amended to require that the medical and genetic histories of prospective adoptees and their relatives be disclosed to prospective adoptive parents.

The persons from whom the parties should collect family history information will depend on the facts and circumstances of each case. However, in all cases, the parties should collect and disclose this information in a manner that respects the privacy of the persons from whom it is obtained and the subjects of the information.[145]

The medical and genetic histories of prospective adoptees and their close relatives may sometimes indicate that a child is at risk for an adult-onset disorder such as Huntington disease. Although, as noted above, it is generally inappropriate to perform genetic tests on prospective adoptees to determine their risks for adult-onset disorders, disclosing existing medical information about the children's risks for such disorders is appropriate. Were such information to be denied to prospective parents and then revealed to the parents after adoption, trust in the adoption system would likely be undermined. The victims of this loss in trust would be the children waiting to be adopted. In addition, we question the practicality of reviewing medical records and excising family history information pertaining to adult-onset disorders.

[145] See N.Y. Soc. Services Law § 373-a (1999) (requiring information identifying a prospective adoptee's birth parents be removed from the child's medical history before that history is shown to prospective adoptive parents).

# Confidentiality of Genetic Information

The principle that health information should be treated confidentially dates at least as far back as the fifth century B.C., when Hippocrates wrote his famous oath.[1] Each physician who took the oath swore that "whatever, in connection with my professional practice, or not in connection with it, I see or hear in the life of men, which ought not be spoken abroad, I will not divulge, as reckoning that all such should be kept secret."[2] The core ethic that physicians should not reveal their patients' confidences remains essentially the same today.[3]

Health information confidentiality[4] has been justified by both utilitarian and rights-based arguments.[5] The most common utilitarian argument is that confidentiality is necessary to promote honest and open communication between physicians and patients, so that physicians can provide proper medical care. Absent such confidentiality, the argument posits, people may avoid seeking necessary medical treatment or provide their physicians incomplete medical histories out of fear that their physicians might disclose medical information that will embarrass them.[6] In addition, a related utilitarian argument

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[1] B. R. Furrow et al., *Health Law*, vol. 1 (St. Paul, MN: West, 1995), 235.

[2] Ibid.

[3] See American Medical Association, Council on Ethical and Judicial Affairs, *Code of Medical Ethics: Current Opinions with Annotations* (Chicago: American Medical Association, 1997), § 5.05 ("The information disclosed to a physician during the course of the relationship between physician and patient is confidential to the greatest possible degree. . . . The physician should not reveal confidential communications or information without the express consent of the patient, unless required to do so by law.").

[4] Some commentators distinguish the right of "confidentiality" from the more general right of "informational privacy." The right of informational privacy is the right to protect personal information against unauthorized access by others. The right of confidentiality, a subset of the right to informational privacy, "refers to an individual's right to prohibit the redisclosure of sensitive information originally disclosed within a confidential relationship (e.g., patient-physician), or otherwise released on assurances that that the information will not be disclosed without consent." M. A. Rothstein, "Genetic Secrets: A Policy Framework," in *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*, ed. M. A. Rothstein (New Haven, CT: Yale University Press, 1997), 451, 453. In this chapter, the term confidentiality is meant to encompass both of these rights.

[5] R. Wachbroit, "International Symposium on Law and Science at the Crossroads: Biomedical Technology, Ethics, Public Policy, and the Law: Rethinking Medical Confidentiality: The Impact of Genetics," *Suffolk University Law Review* 27 (1993): 1391, 1392; D. W. Shuman, "The Origins of the Physician-Patient Privilege and Professional Secret," *Southwestern Law Journal* 39 (1985): 661, 664–666; *Dillinbeck v. Hess*, 73 N.Y.2d 278, 285, 539 N.Y.S.2d 707, 711–712 (1989).

[6] Janlori Goldman, J.D., Director of the Health Privacy Project, Georgetown University Medical Center, Washington, DC, presentation to the New York State Task Force on Life and the Law, March 18, 1998; Wachbroit, "Rethinking Medical Confidentiality," 1392; Shuman, "The Origins of the Physician-Patient Privilege," 664–665; *Dillinbeck*, 73 N.Y.2d at 285, 539 N.Y.S.2d at 712 .

is that the improved dialogue between physicians and patients facilitated by confidentiality protections will increase the accuracy of medical records, thereby making them more useful to researchers who perform retrospective studies.[7] Currently, there is little, if any, empirical data to support either of these contentions.[8]

The major rights-based argument used to justify health information confidentiality is that confidentiality is, in and of itself, a value worth protecting.[9] This argument is based on a desire to preserve the "dignity of the individual" and the sanctity of the private physician-patient relationship.[10]

Virtually all proponents of the utilitarian and rights-based arguments believe that health information confidentiality protections should not be absolute.[11] In certain circumstances, such as where the health or safety of a third party is in serious jeopardy, they agree that exceptions to confidentiality should be made.[12]

Notwithstanding the emphasis on confidentiality in codes of medical ethics, numerous persons and organizations disclose or have access to health and genetic information.[13] For example, the Medical Information Bureau, a private cooperative formed by insurance companies, collects medical information submitted by patients to insurance companies and makes the information available to all of its members.[14] Direct marketers collect health information for their own use or for sale through a variety of methods, including capturing the names of callers to 800 numbers that provide disease information.[15] Self-insured employers, who pool their employees' insurance payments and bear the risk of paying insurance claims, have access to their employees' health information through the insurance claims process.[16] The government has access to vast amounts of health information from, among other sources, newborn screening programs,[17] public hospitals, the Medicare and Medicaid programs, and mandatory reporting by physicians of persons with transmittable conditions, such as tuberculosis,

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[7] Goldman presentation to the Task Force, March 18, 1998.

[8] Ibid.; Shuman, "The Origins of the Physician-Patient Privilege," 664–665; see *Dillinbeck v. Hess*, 73 N.Y.2d at 285, 539 N.Y.S.2d at 712.

[9] Wachbroit, "Rethinking Medical Confidentiality," 1392; Shuman, "The Origins of the Physician-Patient Privilege," 665–666.

[10] Shuman, "The Origins of the Physician-Patient Privilege," 665–666.

[11] Ibid., 663–667.

[12] See ibid.

[13] See, e.g., L. O. Gostin, "Health Information Privacy," *Cornell Law Review* 80 (1995): 451, 485–489; Office of Technology Assessment, "Protecting Privacy in Computerized Medical Information," (1993), Chapter 2, Woodrow Wilson School of Public and International Affairs, Princeton University, website: *http://www.wws.princeton.edu/~ota/ns20/year_f.html*, visited December 30, 1999.

[14] Federal Trade Commission, "Medical Reporting Industry Agrees to Observe FCRA Protections," *FTC Watch* 437 (1995): 1. The member companies provide 80 percent of the health and disability insurance and 99 percent of the life insurance in the United States and Canada. Ibid.

[15] H.R. Rep. 103-601 (1994).

[16] M. A. Rothstein, "Genetic Discrimination in Employment and the Americans with Disabilities Act," *Houston Law Review* 29 (1992): 23, 65–66.

[17] See Chapter 6.

HIV, and AIDS.[18] Moreover, the growing computerization of medical records, which allows for large amounts of individual health information to be stored, manipulated, and transmitted worldwide, has led some commentators to fear that individuals will lose whatever control they might now have over the dissemination of their personal health information.[19]

Most commentators agree that current legal protections against improper disclosure of health and genetic information are woefully inadequate,[20] and surveys indicate that the public concurs. A 1993 Equifax-Harris poll revealed that 80 percent of the public believes that they do not have any control over the use and circulation of their health information.[21] A 1998 survey by the American Medical Association revealed that 68 percent of the public is somewhat or very concerned that their genetic information will be used against them by employers or insurers.[22]

Some commentators claim that genetic information is unlike other health information and should be given special confidentiality protections.[23] Those who espouse this claim, commonly known as genetic exceptionalism,[24] point out that genetic information not only reveals personal health information about individuals but also reveals information that has implications for individuals' families. In addition, because genetic information has "taken on a cultural meaning as the essence of [a] person,"[25] some commentators argue that disclosure of genetic information that indicates that a person may become ill or is a carrier of genes that can cause disease in offspring may lead to individual and familial stigma.[26] Commentators also claim that DNA-based testing, unlike most other medical tests, can predict disease risks decades into the future before any signs or symptoms of diseases are detectable and that it is more precise.[27] Furthermore, some commentators assert that disclosure of genetic information that

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[18] See, e.g., 10 N.Y.C.R.R. §§ 2.1, 2.27 (1999); N.Y. Pub. Health Law § 2130 (McKinney 1999).

[19] Gostin, "Health Information Privacy," 492; Office of Technology Assessment, "Protecting Privacy," Chapter 2.

[20] See, e.g., Department of Health and Human Services, "Confidentiality of Individually Identifiable Health Information: Recommendations of the Secretary of Health and Human Services, Pursuant to Section 264 of the Health Insurance Portability and Accountability Act of 1996," Department of Health and Human Services website: *http://aspe.hhs.gov/admnsimp/pvcrec.htm*, visited December 30, 1999.

[21] Gostin, "Health Information Privacy," 453–454.

[22] American Medical Association, *AMA Survey: Americans Trust Physicians on Genetic Testing Information* (press release, March 11, 1998).

[23] [396] See, e.g., T. H. Murray, "Genetic Exceptionalism and 'Future Diaries': Is Genetic Information Different from Other Medical Information?" in *Genetic Secrets*, 60, 61; Annas, Glantz, and Roche, "The Genetic Privacy Act." For a definition of genetic information, see Chapter 4, page 98.

[24] Ibid. See Chapter 4, page 97.

[25] D. Nelkin and M. S. Lindee, *The DNA Mystique: The Gene as a Cultural Icon* (New York: W. H. Freeman, 1995), 46.

[26] See Chapter 3, page 72.

[27] See Chapter 4, page 99.

indicates a predisposition to disease may result in the denial of employment or insurance coverage.[28] Finally, they argue that genetic information has been used in the past to discriminate and perpetrate terrible horrors against those deemed genetically unfit.[29]

Other commentators believe that the purported differences between genetic information and other health information cannot withstand scrutiny.[30] For example, one commentator notes that information about HIV infection and asymptomatic hepatitis B infection predicts a person's future health in the same way as does genetic information and can be just as stigmatizing.[31] He also points out that information about an individual's chronic common infectious diseases, such as tuberculosis, can be important to family members as it may help them avoid contagion and make life and career choices.[32] In addition, he contends that individuals have been discriminated against for nongenetic health-related reasons.[33] While some commentators who reject genetic exceptionalism admit that "genetic information is unique because it is regarded as unique" by society, they do not believe that these social perceptions justify special confidentiality protections for genetic information.[34]

Maintaining that genetic information should not be treated more confidentially than other health information, the New York State Public Health Council points out that "establish[ing] varying levels of protection for different categories of health information creates difficulties and confusion."[35] Moreover, these differential protections can inadvertently result in disclosure of the very information whose confidentiality is sought to be protected. For example, when responding to requests for patient records that happen to contain HIV-related information, some custodians of records in New York have reportedly stated that they cannot disclose the complete records because they are prohibited by statute from doing so. Because HIV-related information is one of the few types of medical information in New York that receives heightened confidentiality protections, this response creates a red flag that the patient's record likely includes information about HIV.[36] Special protections for genetic information may result in similar types of problems.

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[28] G. Annas, L. Glantz, and P. Roche, *The Genetic Privacy Act and Commentary* (Boston: Boston University School of Public Health, 1996), ii–iii; L. B. Andrews, "Compromised Consent: Deficiencies in the Consent Process for Genetic Testing," *Journal of the American Medical Women's Association* 52 (1997): 39, 39–40. For a discussion of this claim, see Chapter 10.

[29] Annas, Glantz, and Roche, *The Genetic Privacy Act*, ii–iii; E. S. F. Troy, "The Genetic Privacy Act: An Analysis of Privacy and Research Concerns," *The Journal of Law, Medicine and Ethics* 25 (1997): 256, 256–258; Patricia Roche, J.D., Assistant Professor, Boston University School of Public Health, Boston, MA, presentation to the New York State Task Force on Life and the Law, March, 18, 1998.

[30] See, e.g., Murray, "Genetic Exceptionalism," 60–73.

[31] Ibid., 64. For further discussion about the stigmatizing effect of genetic information, see Chapter 4.

[32] Ibid., 65.

[33] Ibid.

[34] Ibid., 71; Rothstein, *Genetic Secrets*, 458–459.

[35] New York State Public Health Council, *Safeguarding the Confidentiality of Health Information* (Albany: New York State Department of Health, 1997) 10, 26. See Rothstein, *Genetic Secrets*, 458.

[36] New York State Public Health Council, *Safeguarding the Confidentiality of Health Information*, 10. An analogous problem has been recognized in federal regulations concerning requests for confidential patient

The National Committee on Vital Health Statistics adds that special protections for specific types of medical information increase the costs of medical records management and may make "the burden on record keepers . . . overwhelming."[37] In addition, some commentators contend that the confidentiality concerns about genetic information can be addressed through laws that mandate a high level of protection for all health information.[38]

## Federal Constitutional Law

The government obtains genetic information about individuals through a variety of methods, including mandatory genetic testing. For example, a vast majority of states have newborn screening programs that require physicians to submit bloodspots from newborns to government laboratories for testing for specific genetic diseases.[39] Moreover, although it no longer appears to be enforced, New York State law requires applicants for marriage licenses who are "not of the Caucasian, Indian, or Oriental races" to be tested "as may be necessary," for sickle cell disease and informed of the results.[40] In addition, although it is not health related, more than forty states, as well as the federal government, perform genetic identification testing on convicted criminals in order to identify them in the future should they commit additional crimes and leave biological evidence behind.[41] The federal government also collects and stores blood samples from all members of the armed forces so that their remains can be identified using genetic identification testing, if other means of identification fail.[42]

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alcohol and drug records. See 42 C.F.R. § 2.13(c)(2) (1999) (requiring that "[a]ny answer to a request for a disclosure of patient records which is not permissible under these regulations must be made in a way that will not affirmatively reveal that an identified individual has been, or is being diagnosed or treated for alcohol or drug abuse").

[37] National Committee on Vital Health Statistics, *Health Privacy and Confidentiality Recommendations* (Washington, D.C.: National Committee on Vital Health Statistics, 1997), Section M, National Committee on Vital Health Statistics website: *http://aspe.os.dhhs.gov/Ncvhs/privrecs.htm*, visited September 15, 1998.

[38] See, e.g., ibid.

[39] See, e.g., N.Y. Pub. Health Law § 2500-a (McKinney 1999). For further discussion of newborn screening, see Chapter 6.

[40] N.Y. Dom. Rel. Law § 13-aa(1) (McKinney 1999). The law provides that a marriage license cannot be denied because of a positive test result and that the absence of the test does not invalidate a marriage. See also Ga. Stat. § 19-3-40 (1999) (requiring syphilis testing prior to marriage and that the results be shown to a probate judge).

[41] See, e.g., N.Y. Exec. Law §§ 995-c(1), 995-c(3) (McKinney 1999); *Rise v. Oregon*, 59 F.3d 1556, 1558 (9th Cir. 1995). For a discussion of genetic testing to determine a person's identity, see Chapter 2, page 31.

[42] See *Mayfield v. Dalton*, 901 F. Supp. 300, 302 (D. Haw. 1995), *vacated on other grounds*, 109 F.3d 1423 (9th Cir. 1997). The government usually stores service members' blood samples for fifty years, but will destroy the samples after the individuals complete their military obligations if they so request. See *Mayfield*, 109 F.3d at 1425–1426. See also C. Smith, "Navy Man Prevails in Blood-Test Dispute:

It is possible that the state or federal governments will mandate additional genetic testing in the future. For example, they might do so in their roles as employers to determine whether the employees are susceptible to environmental hazards at their workplaces. New York law specifically permits employers to mandate such testing as a condition of employment.[43]

**The Right against Unreasonable Searches and Seizures**

The fourth amendment to the United States Constitution prohibits federal, state, and local governments from performing "unreasonable" searches and seizures of "persons, houses, papers and effects."[44] This prohibition gives individuals the right to keep their information and activities shielded from government scrutiny and "prevent[s] invasions of dignitary interests."[45]

In most instances, the government's collection of biological samples for genetic testing constitutes a search within the meaning of the fourth amendment.[46] In addition, the chemical and biological analysis of samples that the government has acquired legally

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Technician Reinstated after Losing His Job over Refusal of DNA Sample," *Seattle Post-Intelligencer*, September 16, 1997.

[43] See N.Y. Exec. Law § 296(19) (McKinney 1999).

[44] U.S. Const. Amend. IV. See, e.g., *Skinner v. Ry. Labor Executives Ass'n*, 489 U.S. 602, 613–614, 619, 109 S. Ct. 1402, 1411, 1414 (1989). In general, the fourth amendment does not apply to private parties. See *Chandler v. Miller*, 520 U.S. 305, 323, 117 S. Ct.. 1295, 1305 (1997).

[45] W. R. LaFave, *Search and Seizure: A Treatise on the Fourth Amendment* (St. Paul, MN: West, 1996, and Pocket Part, 1998), § 2.1(b) n.59.1 (internal quotation marks omitted).

[46] While the government's acquisition of body tissues also can be characterized as a seizure, the privacy interests at stake "are adequately taken into account by [the] conclusion that such [acquisitions] are searches." *Skinner*, 489 U.S. at 617, 109 S. Ct. at 1413. The Supreme Court has held that the government's acquisition of blood samples, urine samples, breath samples, and fingernail scrapings are searches. See *Skinner*, 489 U.S. at 616–618, 109 S. Ct. at 1412–1413 (blood, urine, and breath samples); *Cupp v. Murphy*, 412 U.S. 291, 295, 93 S. Ct. 2000, 2003 (1973) (fingernail scrapings). Most courts also have held that the government's acquisition of saliva samples is a search. See, e.g., *United States v. Nicolosi*, 885 F. Supp. 50, 55–56 (E.D.N.Y. 1995) (government's use of a cheek swab in the defendant's mouth to collect saliva and requiring the defendant to expectorate saliva into a receptacle are both searches); *Commonwealth v. Blasioli*, 454 Pa. Super. 207, 217, 685 A.2d 151, 155–156 (Pa. Super. Ct. 1996) (having a defendant expectorate saliva is a search); *People v. Standen*, 95 Misc.2d 907, 909, 408 N.Y.S.2d 678 (N.Y. Cty. Ct. 1978). Courts are divided over whether the acquisition of hair samples implicates the fourth amendment's protections. Compare, e.g., *Matter of Barber v. Rubin*, 72 A.D.2d 347, 352–353, 424 N.Y.S.2d 453, 457–458 (N.Y. App. Div. 1980) (extraction of hair and its roots is a search); *State v. Kilmer*, 190 W. Va. 617, 628 n. 13, 439 S.E.2d 881, 892 n.13 (W. Va. 1993) (same); *In re Mills*, 686 F.2d 135, 141–143 (3rd Cir.) (Gibbons, J. Concurring) (1982) (removal of hair above the skin surface is a search), *cert. denied*, 459 U.S. 1021, 103 S. Ct. 386 (1982) with *In re Mills*, 686 F.2d at 139–140 (majority opinion) (removal of hair above the skin surface is not a search and does not implicate fourth amendment protections); *United States v. Nicolosi*, 885 F. Supp at 55 ("Obtaining [hair] samples does not implicate any privacy or dignitary interests and can be affected without a full Fourth Amendment procedure."). See also *United States v. D'Amico*, 408 F.2d 331, 332–333 (2d Cir. 1969) (clipping of hair may be a "seizure," but the intrusion is so minimal that it does not implicate fourth amendment protections).

also may be searches. The Supreme Court has strongly suggested that the chemical and biological analysis of urine and blood for drugs and alcohol are searches because they

disclose information concerning the state of the sample source's body.[47] Nevertheless, lower courts remain divided on this issue.[48] The Supreme Court also has suggested, and lower courts have held, that the analysis of biological samples to ascertain a person's health and genetic information implicates fourth amendment privacy interests that are weightier than the interests implicated by blood or urine analysis to detect the use of drugs or alcohol.[49]

For example, in *Norman-Bloodsaw v. Lawrence Berkeley Laboratories*,[50] employees of a federal laboratory provided blood samples to the laboratory as part of their mandatory medical exams. Without the employees' knowledge or consent, the laboratory tested their blood for sickle cell trait, syphilis, and pregnancy.[51] In ruling that the testing violated the employees' fourth amendment rights, the United States Court of Appeals for the Ninth Circuit emphasized that consent to a general medical examination or to give blood or urine samples "does not abolish one's privacy right not to be tested for intimate, personal matters involving one's health."[52] The court observed that "one can think of few subject areas more personal and more likely to implicate privacy interests than that of one's health or genetic makeup."[53]

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[47] See *Vernonia School Dist. 47J v. Acton*, 515 U.S. 646, 658, 115 S. Ct. 2386, 2393 (1995) (drug analysis performed on urine is, in and of itself, an invasion of privacy); *Skinner*, 489 U.S. at 616–18, 109 S. Ct. at 1412–1414 (holding that the collection and chemical analysis of urine are separate fourth amendment searches).

[48] Compare *Norman-Bloodsaw v. Lawrence Berkeley Laboratory*, 135 F.3d 1260, 1269–1270 and n.13 (9th Cir. 1998) (biological analysis of legally obtained blood samples is a search); *In the Matter of J.W.K.*, 574 N.W.2d 103, 105 (Minn. Ct. App.) (citing cases), *rev'd on other grounds*, 583 N.W.2d 752 (Minn. 1998); *State v. Copeland*, 680 S.W.2d 327, 329 (Mo. Co. App. 1984) with *People v. King*, 232 A.D.2d 111, 117–118, 663 N.Y.S.2d 610, 614–615 (N.Y. App. Div. 1997) (holding that once the government has lawfully obtained a blood sample from a person, "the scientific analysis of [the] sample does not involve any further search or seizure of the defendant's person"). See also *People v. Daniels*, 73 Cal. Rptr.2d 399, 404–405 (Cal. Ct. App. 1998) (although blood typing performed on blood lawfully obtained was a search, it was justified without a warrant because it was a minimal intrusion and would be used to determine whether the subject should remain a suspect in a crime).

[49] See *Vernonia*, 515 U.S. at 658, 115 S. Ct. at 2393 (indicating that urinalysis to determine health status is a greater invasion of privacy than urinalysis used to detect drugs); *Norman-Bloodsaw*, 135 F.3d at 1269–1270.

[50] 135 F.3d 1260 (9th Cir. 1998).

[51] Ibid., 1265.

[52] Ibid., 1270.

[53] Ibid., 1269.

Determining that government actions are searches or seizures is only the first step in a fourth amendment analysis. The next is to determine whether the searches or seizures are "reasonable."[54] Outside of the criminal context, the government may perform searches without a warrant or individualized suspicion of wrongdoing if (1) "special needs" beyond the normal need for law enforcement make the warrant and probable cause requirement impracticable"[55] and (2) "the privacy interests implicated by the search are minimal."[56]

Utilizing this "special needs" analysis, the Supreme Court has upheld, absent individualized suspicion, warrantless collections of urine samples for drug testing from railway employees involved in train accidents, customs officers seeking promotions, and high school students who engage in interscholastic athletic competitions.[57] However, because the Court appears to have assigned greater weight to the privacy interests implicated by the analysis of biological samples for health and genetic information,[58] the results of these cases may not be good predictors of how courts will rule on fourth amendment challenges to government-mandated genetic testing.

Although the fourth amendment may prevent the government from obtaining medical and genetic information from the subject of that information, it probably does not prevent the government from obtaining the same information from third parties. In *Miller v. United States*,[59] the Supreme Court observed that, even if an individual gives a third party information "on the assumption that it [would] be used only for a limited purpose and the confidence placed in the third party [would] not be betrayed," the fourth amendment does not prevent the government from compelling the third party to disclose

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[54] Except in certain delineated circumstances, searches and seizures in the criminal context are considered "reasonable" only if they are authorized by a judicial warrant based on probable cause that an individual has committed a crime, see *Skinner*, 489 U.S. at 618–619, 109 S. Ct. 1413–1414, or that the property that the government seeks to investigate are "fruits, instrumentalities or evidence" of crimes. See, e.g., *Zurcher v. Stanford Daily*, 436 U.S. 547, 556–557, 98 U.S. 1970, 1976–1977 (1978).

[55] See *Vernonia*, 515 U.S. at 653, 115 S. Ct. at 2386; *Skinner*, 489 U.S. at 619, 109 S. Ct. at 1414. The special needs "must be substantial — important enough to override the individual's acknowledged privacy interest, sufficiently vital to suppress the Fourth Amendment's normal requirement of individualized suspicion." *Chandler*, 520 U.S. at 318, 117 S. Ct. at 1303. The warrant and probable cause requirements are impracticable where "an important governmental interest furthered by the intrusion would be placed in jeopardy by a requirement of individualized suspicion." See *Chandler*, 520 U.S. at 314, 117 S. Ct. at 1301; *Skinner*, 489 U.S. at 624, 109 S. Ct. at 1417. "[B]eyond the normal need for law enforcement" means "concerns other than crime detection." *Chandler*, 520 U.S. at 305, 117 S. Ct. at 1296.

[56] The Supreme Court has also upheld searches without individualized suspicion in a number of other circumstances, including searches at fixed border checkpoints and sobriety checkpoints as well as "administrative inspections in 'closely regulated' businesses.'" *Chandler*, 520 U.S. at 308, 117 S. Ct. at 1298.

[57] *Chandler*, 520 U.S. at 308–309, 117 S. Ct. at 1298. In *Chandler*, the Supreme Court, utilizing the special needs analysis, held that a Georgia law that required drug testing of all candidates for state office violated the fourth amendment.

[58] See page 247, this chapter.

[59] 425 U.S. 435, 96 S. Ct. 1619 (1976).

the information.[60] The Supreme Court has not ruled on the applicability of this reasoning to health or genetic information held by third parties.

A number of state courts, including one New York appellate court, have ruled that individuals cannot rely on the fourth amendment to prevent the government from obtaining from private hospitals the results of blood alcohol tests that have been performed for medical reasons.[61] Nevertheless, two of these courts specifically left open the question whether individuals have a reasonable expectation of privacy in their general medical records held by third parties.[62] Other courts have ruled that subjects of private blood alcohol tests may utilize fourth amendment protections to prevent the government from obtaining the results because the subjects have a reasonable expectation of privacy in their medical records even when the records are held by third parties.[63]

**The Right to Informational Privacy**

In *Whalen v. Roe*,[64] the Supreme Court held that the due process clause protects individuals' interest in "avoiding disclosure of personal matters."[65] *Whalen* concerned the constitutionality of a New York statute that required doctors and pharmacists to send copies of completed prescription forms to the New York State Department of Health. The forms identified the prescribing doctors; the patients' names, addresses, and ages; the dispensing pharmacies; and the drugs and dosages.[66] The department saved the information on computer tapes, which were stored in a secured area.[67] The purpose of the statute was to prevent abuses in the prescribing and dispensing of certain prescription drugs.[68]

The plaintiffs claimed that the required disclosure of their prescription information to the health department, and the resultant risk that that information might improperly be disclosed to others, violated their constitutional rights. The Supreme Court

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[60] Ibid., 425 U.S. at 443, 96 S. Ct. at 1624. Accord, e.g., *United States v. Jacobsen*, 466 U.S. 109, 117, 104 S. Ct. 1652, 1658 (1984).

[61] See, e.g., *People v. Ameigh*, 95 A.D.2d 367, 367–369, 467 N.Y.S.2d 718, 718–719 (N.Y. App. Div. 1983); *State v. Hardy*, 963 S.W.2d 516, 523–527 (Tex. Crim. App. 1997) (citing cases); *Tims v. State*, 711 So.2d 1118, 1122–1124 (Ala. Crim. App. 1997); *People v. Perlos*, 436 Mich. 305, 329, 462 N.W.2d 310, 321 (Mich. 1990).

[62] *State v. Hardy*, 963 S.W.2d at 527; *People v. Perlos*, 436 Mich. at 330, 462 N.W.2d at 321.

[63] See *Commonwealth v. Riedel*, 539 Pa. 172, 175–183, 651 A.2d 135, 137–141 (Pa. 1994); *State v. Copeland*, 680 S.W.2d 327, 328–331 (Mo. App. 1984).

[64] 429 U.S. 589, 97 S. Ct. 869 (1977).

[65] *Whalen v. Roe*, 429 U.S. 589, 599, and n.25, 97 S. Ct. 869, 876, and n.25 (1977). Accord *Nixon v. Adm'r of Gen. Serv.*, 433 U.S. 425, 457–458, 97 S. Ct. 2777, 2797 (1977).

[66] See *Whalen*., 429 U.S. at 593 and n.10, 97 S. Ct. at 873 and n.10.

[67] See ibid., 429 U.S. at 593–595 and n.12, 97 S. Ct. at 873–874 and n.12.

[68] See ibid., 429 U.S. at 591–592, 97 S. Ct. at 872–873.

disagreed. While recognizing that the due process clause protects individuals' right to avoid disclosure of personal matters, the Court ruled that the statute was constitutional because it did not "pose a sufficiently grievous threat [to the plaintiffs' privacy] interest[s] to establish a constitutional violation."[69]

Since *Whalen*, numerous courts have found a constitutional right to informational privacy in health information.[70] For example, in *Doe v. Southeastern Pennsylvania Transportation Authority,*[71] the chief administrative officer of a public transportation authority learned that the plaintiff was HIV positive through a review of the authority's

prescription drug plan. She then disclosed that information to other authority employees.[72] The court ruled that the plaintiff had "a constitutional right to privacy in his prescription drug records," although it held that, under the particular facts of the case, the plaintiff's right had not been violated.[73]

The right to informational privacy is not absolute, and its boundaries are unclear. Most courts have ruled that the first step in ascertaining whether the government's acquisition or disclosure of personal information violates the individual's right to informational privacy is to determine whether the government's interest in acquiring or disseminating the information is "substantial."[74] The second step is to weigh the individual's privacy interest against the government's interest in acquiring or disclosing

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[69] Finding no evidence that the security provisions in the New York statute and regulations were not being followed, the Court concluded that requiring the disclosure of prescription information "to the representatives of the State having responsibility for the health of the community, does not automatically amount to an impermissible invasion of privacy." Ibid., 429 U.S. at 602–604, 97 S. Ct. at 877–878.

[70] See, e.g., *Doe v. Southeastern Pennsylvania Transp. Auth.*, 72 F. 3d 1133, 1137–1138 (3rd Cir. 1995) (medical records); *Doe v. City of New York*, 15 F.3d 264, 267–270 (2d Cir. 1994) (HIV status). But see *Am. Fed'n of Gov't Employees v. Dep't of Hous. & Urban Dev.,* 326 U.S. App. D.C. 185, 190–192, 118 F.3d 786, 791–793 (D.C. Cir. 1997) (dictum) (doubting "the existence of a constitutional right of privacy in the nondisclosure of personal information" ). See also *Kallstrom v. City of Columbus*, 136 F.3d 1055, 1060–1062 and n.1 (6th Cir. 1998) (holding that there is an informational privacy right only when the individual privacy interest is of "constitutional dimension," i.e., "it implicate[s] a fundamental liberty interest").

[71] 72 F. 3d 1133 (3rd Cir. 1995).

[72] Ibid., 1135–1137.

[73] Ibid., 1137–1143.

[74] See, e.g., *South Eastern Pennsylvania*, 72 F.3d at 1139–1140; *Doe v. City of New York*, 15 F.3d at 269–270. Other courts have ruled that the reasons justifying the disclosure must be compelling. See, e.g., *Sheets v. Salt Lake County*, 45 F.3d 1383, 1387–1388 (10th Cir. 1995); *Walls v. City of Petersburg*, 895 F.2d 188, 192–193 (4th Cir. 1990). Cf. *DiPalma v. Phelan*, 81 N.Y.2d 754, 756, 593 N.Y.S.2d 778, 778–779 (1992) (holding that a police officer did not violate any clearly established privacy rights of a woman when he disclosed to a town board that she had been sexually abused by her father, a town employee, when she was less than eighteen years old; the town had a "legitimate government interest" in assessing the fitness of one of its employees and courts had not at the time of the disclosure determined that disclosures under such circumstances would violate privacy rights).

the information at issue.[75] In a number of cases, the individual's privacy interests have prevailed.[76]

Courts are split on the issue of whether an individual's right to informational privacy is implicated when the government acquires information about the individual from a third party.[77] Moreover, while at least two courts have ruled that family members sometimes have informational privacy interests in one another's personal information,[78] no court has ruled on what, if any, informational privacy rights a family member may have in the genetic information of other family members.

**Remedies**

Individuals whose constitutional rights have been violated by the government can sue for compensatory and punitive damages, as well as injunctive relief.[79] In addition, successful plaintiffs are entitled to attorneys' fees.[80]

## New York State Constitutional Law

On a number of occasions, the New York Court of Appeals has interpreted the New York State Constitution to provide broader protections of individual rights than the federal constitution.[81] These additional protections, which do not apply to the federal

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[75] *Doe v. City of New York*, 15 F.3d at 269–270. See, e.g., *Nat'l Treasury Employees Union v. United States Dept. of the Treasury*, 25 F.3d 237, 242–243 and n.2 (5th Cir. 1994).

[76] *Doe v. Borough of Barrington*, 729 F. Supp. 376 (D.N.J. 1990); *Carter v. Broadlawns Medical Center*, 667 F. Supp. 1269, 1282 (S.D. Iowa 1987) (court barred hospital from disclosing to hospital chaplains patients' medical records because the disclosures violated the patients' rights to informational privacy). See also *Norman-Bloodsaw*, 135 F.3d at 1275 (refusing to dismiss complaint that alleged that the government had improperly acquired health and genetic information by performing blood tests without consent).

[77] Compare *United States v. Westinghouse Elec. Corp.*, 638 F.2d 570 (3rd Cir. 1980) (employees' right to informational privacy implicated by government subpoena to employer for employees' medical records) with *Barber v. Winn*, 1997 WL 151999, *3 (N.D.N.Y. 1997)(holding that, because the plaintiffs turned over their financial records to a third party, they had no informational privacy interest in them).

[78] See *Sheets*, 45 F.3d at 1387–1388 (husband has an informational privacy interest in the portions of his deceased wife's diary that contained information about him); *Doe v. Borough of Barrington*, 729 F. Supp. at 384–385 (family of person with AIDS, whose disease status had been disclosed publicly by the government, could sue the government for violation of their privacy rights because "revealing that one's family or household member has AIDS causes the entire family to be ostracized").

[79] 42 U.S.C.A. § 1983 (West 1998); *Bivens v. Six Unknown Named Agents of the Fed. Bureau of Narcotics*, 403 U.S. 388, 394–396, 91 S. Ct. 1999, 2004–2005 (1971). Injunctive relief usually comes in the form of an order by a court either prohibiting a party from performing an act or ordering a party to perform an act. See *Black's Law Dictionary* (St. Paul, MN: West, 1979), 368. For example, a court might prohibit a state agency from releasing private information.

[80] See 42 U.S.C. § 1988(b) (1994 & Supp. III 1997).

[81] See, e.g., *People ex rel. Arcara v. Cloud Books, Inc.*, 68 N.Y.2d 553, 510 N.Y.S.2d 844 (1986) (holding that the New York State Constitution's guarantee of freedom of expression provides greater protection than

government, shield New Yorkers from conduct by representatives of the state government that would be permissible under the U.S. Constitution.

Article I, Section XII of the New York State Constitution, which is the state constitution's counterpart to the fourth amendment, protects individuals against unreasonable searches and seizures. The New York Court of Appeals has interpreted ection XII as providing greater protection against searches and seizures than the fourth amendment.[82]

In the criminal context, the Court of Appeals has held that, absent exigent circumstances, Article I, Section XII prohibits the government from searching a person's body for biological samples without probable cause and a warrant.[83] The court has emphasized that "when the physical evidence whose possession is the raison d'être for detaining a person cannot be altered or destroyed, as in the case of the type of blood integral to one's body, by definition there can be no exigency to justify exemption from the warrant standard of probable cause."[84] Therefore, because individuals cannot alter or destroy their DNA, it is reasonable to assume that in the criminal context, Section XII requires the state government to procure a warrant based on probable cause before it may obtain biological samples from individuals' bodies and perform genetic tests on the samples.

In the civil arena, the Court of Appeals has held that under Section XII, "random searches conducted by the State without reasonable suspicion are closely scrutinized, and generally only permitted when the privacy interests implicated are minimal, the government's interest is substantial, and safeguards are provided to insure that the individual's reasonable expectation of privacy is not subjected to unregulated discretion."[85] Using this test, the Court of Appeals struck down a program that required all probationary teachers to submit to urinalysis for the presence of drugs.[86] However, the court has upheld programs that required correction officers and police officers in units specializing in drug interdiction to submit to urinalysis for the presence of drugs.[87] The

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the first amendment to the United States Constitution). See generally E. R. Alexander, "The Right to Privacy and the New York State Constitution: An Analytical Framework," *Touro Law Review* 8 (1992): 725.

[82] See, e.g., *People v. Scott*, 79 N.Y.2d 474, 496–497, 583 N.Y.S.2d 920, 933935 (1992); *People v. Alvarez*, 70 N.Y.2d 375, 378, 521 N.Y.S.2d 212, 213 (1987).

[83] See *Matter of Abe A.*, 56 N.Y.2d 288, 295–296, 425 N.Y.S.2d 6, 10 (1982).

[84] Ibid. In addition to Section XII, the Court of Appeals also cited the fourth amendment as support for its conclusion.

[85] *Matter of Patchogue-Medford Congress of Teachers v. Bd. of Educ.*, 70 N.Y.2d 57, 70, 517 N.Y.S.2d 456, 462 (1987). Accord *Matter of Delaraba v. Nassau County Police Dept.*, 83 N.Y.2d 367, 370–371, 610 N.Y.S.2d 928, 929–930 (1994).

[86] See *Patchogue-Medford*, 70 N.Y.2d 57, 517 N.Y.S.2d 456.

[87] See *Matter of Delaraba v. Nassau County Police Dept.*, 83 N.Y.2d at 370–371, 610 N.Y.S.2d at 929–930 (police officers in drug interdiction units); *Matter of Caruso v. Ward*, 72 N.Y.2d 432, 442 N.Y.S.2d 142 (1988) (same); *Matter of Seelig v. Koehler*, 76 N.Y.2d 87, 556 N.Y.S.2d 832 (1990) (correction officers), *cert. denied*, 498 U.S. 847, 111 S. Ct. 134 (1990).

court has not had an opportunity to apply this reasoning to warrantless and suspicionless acquisitions of health or genetic information.

### Remedies

Individuals who believe that their Section XII rights against unreasonable searches and seizures have been violated by the state government can sue for damages and injunctive and declaratory relief.[88]

## Federal Statutes and Regulations

The federal government has yet to enact a comprehensive statute or set of regulations concerning health information confidentiality. What exist are statutes and regulations that limit the disclosure and acquisition of health information in particular circumstances.

### The Health Insurance Portability and Accountability Act

As part of the Health Insurance Portability and Accountability Act of 1996, Congress provided that, unless confidentiality legislation concerning individually identifiable health information was enacted by 1999, the Secretary of the Department of Health and Human Services would be empowered to issue regulations on the confidentiality of individually identifiable health information that is or has been stored in an electronic format.[89] On October 29, 1999, the Secretary issued proposed regulations concerning this subject. These proposed regulations apply to certain health care entities, including employers that act as health plans and/or health care providers for their employees.[90] However, the proposed regulations do not apply to other employers and entities that might come into possession of individually identifiable health information.[91] The proposed regulations are currently subject to a comment period, after which the Secretary will issue final regulations.

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[88] See *Brown v. New York*, 89 N.Y.2d 172, 186–189, 652 N.Y.S.2d 223, 232–235 (1996). Declaratory relief, most often referred to as a declaratory judgment, is a "binding adjudication of the rights and status of litigants even though no consequential relief is awarded." *Black's Law Dictionary*, 368. For example, a person who wishes to perform an act arguably prohibited by a statute may ask the court for a declaration that the statute does not prohibit the act.

[89] Health Insurance Portability and Accountability Act, P.L. 104-191 § 264 (1996); 42 U.S.C.A. § 1320d-2 note (West 1999).

[90] M. R. Anderlick, "Responsibilities of Employers Under Proposed Privacy Rule," University of Houston Law Center, Houston, TX, website: *http://www.law.uh.edu/healthlawperspectives/Privacy/991216Responsibilities.html*, visited December 29, 1999.

[91] See ibid.

**The Privacy Act**

The Privacy Act[92] regulates the collection, maintenance, use, and disclosure of information that federal agencies acquire about individuals.[93] As a general rule, the Privacy Act permits federal agencies to disclose an individual's personal information only with that individual's written request or informed consent.[94] Courts have held that the Privacy Act covers medical records maintained by federal agencies.[95]

Willful violators of the Privacy Act can be sued for compensatory damages and attorneys' fees.[96] In addition, willful violators of the Privacy Act who improperly disclose agency records that contain "individually identifiable information" are subject to criminal misdemeanor prosecution and can be fined up to $5,000.[97]

The Privacy Act contains at least two significant exceptions. First, the Privacy Act generally permits intragency disclosure of protected records to "officers and employees of the agency which maintains the record who have a need for the record in the performance of their duties."[98] This exception allows virtually unfettered intragency disclosure of records within federal agencies.[99]

Second, the Privacy Act permits agencies to disclose personal information for a "routine use"[100] — a use of the records "for a purpose which is compatible with the purpose for which it was collected" — as long as the agencies publish a notice of the intended use in the Federal Register.[101] According to a congressional report, most federal agencies have incorrectly interpreted the routine use provisions as permitting them to disclose almost any personal information as long as they publish the required notice.[102] Federal health agencies have utilized the routine use exception to justify the release of personally identifiable health information.[103] However, in at least one case, a federal appeals court rejected a Veterans Administration Hospital's reliance on the routine use provisions to justify its disclosure of medical records in response to a grand jury subpoena. The court ruled that the disclosure was not "compatible with the purpose for which the record was collected."[104]

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[92] 5 U.S.C. § 552a (West 1999).
[93] See H.R. Rep. 103-601 (1994).
[94] See ibid., § 552a(b); Gostin, "Health Information Privacy," 500.
[95] See *Doe v. DiGenova*, 250 U.S. App. D.C. 274, 278–287, 779 F.2d 74, 79–87 (D.C. Cir. 1985); *United States v. Trabert*, 978 F. Supp. 1368, 1375–1376 (D. Colo. 1997).
[96] 5 U.S.C.A. § 552a(g) (West 1999).
[97] Ibid., § 552a(i)(1). Thus far, there is only one reported case of a criminal prosecution under the Privacy Act. That case involved the disclosure of medical records and ended in an acquittal. See *Trabert*, 978 F. Supp. at 1375–1379.
[98] 5 U.S.C.A. § 552a(b)(1) (West 1999); H.R. Rep. 103-601 (1994).
[99] See H.R. Rep. No. 103-601 (1994).
[100] 5 U.S.C.A. § 552(b)(3) (West 1999).
[101] Ibid., §§ 552a(a)(7), 552a(e)(4)(D), 552a(e)(11).
[102] H.R. Rep. 103-601 (1994).
[103] Gostin, "Health Information Privacy," 501.
[104] See *Doe v. Stephens*, 271 U.S. App. D.C. 230, 239, 851 F.2d 1457, 1467 (D.C. Cir. 1988).

### The Americans with Disabilities Act

The Americans with Disabilities Act (ADA) prohibits employers from discriminating against employees or potential employees based on disability.[105] Under certain circumstances, the ADA allows employers to require employees and potential employees to undergo medical examinations and to answer questions about their medical histories. Subject to a number of exceptions, the ADA mandates that the information obtained about the medical conditions and medical histories of their employees as a result of these examinations must be kept "confidential" and in separate medical files.[106]

For example, in *Downs v. Massachusetts Bay Transportation Authority*,[107] the plaintiff, a bus driver, falsely indicated on a pre-employment medical history form that he had never received workers' compensation and had never had joint pains. After the plaintiff was hired, he was hospitalized with a tendon problem. The plaintiff subsequently filed a worker's compensation claim, and the employer released the plaintiff's medical history form to a claims investigator. The investigator determined that the plaintiff had lied on the form, the employer fired the plaintiff, and the plaintiff sued the defendant under the ADA.[108] The court ruled that the employer had violated the confidentiality provisions of the ADA when it disclosed the plaintiff's medical history form to the claims investigator.[109]

Individuals who believe that their employers or potential employers have violated their confidentiality rights under the ADA can sue for injunctive relief, compensatory damages, punitive damages, and attorneys' fees.[110] However, the ADA applies only to employers who have fifteen or more employees.[111]

### The Fair Credit Reporting Act

Congress enacted the Fair Credit Reporting Act (FCRA) to regulate the creation and disclosure of "consumer reports" by "consumer reporting agencies."[112] A consumer report includes "any written, oral, or other communication of any information by a

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[105] 42 U.S.C.A. § 12111 (West 1998).
[106] See 42 U.S.C.A. §§ 12112(d)(3)(B), 12112(d)(4)(C) (1998); 29 C.F.R. §§ 1630.14(b)(1), 1630.14(c)(1) (West 1998).
[107] 13 F. Supp.2d 130 (D. Mass. 1998).
[108] Ibid., at 130–133.
[109] Ibid., at 141–142. See also *Cossette v. Minnesota Power & Light*, 188 F.3d 964, 969–970 (8th Cir. 1999) (permitting ADA lawsuit to go forward against the plaintiff's former employer for improperly disclosing the results plaintiff's medical examination).
[110] 42 U.S.C.A. § 12117(a) (West 1999).
[111] Ibid., § 12111(5)(A).
[112] See *Cisneros v. U.D. Registry, Inc.*, 39 Cal. App. 4th 548, 559 (Cal. App.4th 1995).

consumer reporting agency bearing on a consumer's" personal characteristics "which is used or expected to be used or collected in whole or in part for the purpose of serving as a factor in establishing the consumer's eligibility for credit or insurance to be used primarily for personal, family, or household purposes and employment purposes."[113] Unless the subject of a consumer report consents, the FCRA explicitly prohibits consumer reporting agencies from disclosing "for employment purposes, or in connection with a credit transaction or a consumer transaction or a direct marketing transaction," consumer reports that contain "medical information."[114] Individuals who believe that their rights under the FCRA have been violated can sue the alleged violators for compensatory and, in some circumstances, punitive damages.[115]

The FCRA's medical information protection has a number of limitations. First, the FCRA applies only to the disclosure of medical information by consumer reporting agencies, and that limitation excludes many persons who have access to health information.[116] Second, the act exempts from its coverage "any report based on the reporter's first-hand experience of the subject" of the report,[117] and thus it is arguable that the FCRA would not prohibit physicians and genetic testing laboratories from disclosing their patients' or clients' health and genetic information.[118]

## The Gramm-Leach-Bliley Act

The Gramm-Leach-Bliley Act, which President Clinton signed into law in 1999, regulates the disclosure by financial institutions of personally identifiable financial information that consumers provide to these institutions or that these institutions otherwise obtain.[119] Financial institutions include insurers,[120] and recent regulations have interpreted the Gramm-Leach-Bliley Act as covering virtually all information, including

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[113] 15 U.S.C.A. 1681a(d)(1) (West 1999). A "consumer reporting agency" is "any person which, for monetary fees, dues, or on a cooperative nonprofit basis, regularly engages in whole or in part in the practice of assembling or evaluating consumer credit information or other information on consumers for the purpose of furnishing consumer reports to third parties, and which uses any means or facility of interstate commerce for the purposes of preparing or furnishing consumer reports." Ibid., § 1681a(f).

[114] 15 U.S.C.A. § 1681b(g) (West 1999). Medical information is defined as "information or records obtained, with the consent of the individual to whom it relates, from licensed physicians or medical practitioners, hospitals, clinics, or other medical or medically related facilities." Ibid., § 1681a(i). Prior to the 1996 amendment that added this prohibition, at least one federal appeals court ruled that "medical-type" reports that are used to determine employment are consumer reports because they are communications that bear upon "personal characteristics." *Hodge v. Texaco, Inc.*, 975 F.2d 1093, 1095–1096 (5th Cir. 1992).

[115] 15 U.S.C.A. §§ 1681n, 1681o (West 1999).

[116] For a discussion of the number and types of individuals and organizations that have access to health information, see page 242, this chapter.

[117] *Hodge v. Texaco, Inc.*, 975 F.2d at 1096. See 15 U.S.C.A. § 1681a(d)(2)(A) (West 1999).

[118] See *Hodge v. Texaco, Inc.*, 975 F.2d at 1096–1097 (report of results of urinalysis performed by a laboratory on an individual was not a "consumer report" because the laboratory performed the urinalysis itself).

[119] See 15 U.S.C.A. §§ 6809(4)(A)(i), (iii) (West 2000)

[120] Ibid., § 6809(3)(A); 12 U.S.C.A. § 1843(k)(B) (West 2000).

health information, that consumers provide to financial institutions.[121] The act will become effective November 12, 2000, unless regulations interpreting the act specify a later effective date.[122]

The Gramm-Leach-Bliley Act requires financial institutions to inform consumers about the institutions' privacy policies and practices, including the circumstances under which the institutions will disclose consumers' nonpublic personal information to nonaffiliated third parties.[123] The act also requires financial institutions to give consumers the opportunity to opt out of such disclosures before the institutions make them.[124] Finally, the act prohibits nonaffiliated third parties, who receive individuals' nonpublic personal information from financial institutions, from disclosing that information to anyone, unless the disclosure would be lawful if made by the financial institution.[125]

The act authorizes various federal agencies to issue regulations and enforce the act against certain financial institutions and the act authorizes state insurance authorities to enforce the act against insurers.[126]

## New York State Statutes, Regulations, and Common Law

Traditionally, the law did not safeguard the confidentiality of physician-patient communications,[127] although the courts did recognize that a physician who voluntarily revealed a patient's confidences without being ordered to do so by a court would, in the words of a 1776 English case, "be guilty of a breach of honor and of great indiscretion."[128] Since then, New York, like most other states, has enacted numerous statutes and regulations that protect the confidentiality of health and genetic information in many different settings.[129]

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[121] See, e.g., 16 C.F.R. § 313(o)(1)(i) (2000).

[122] Pub. L. 106-102, Title V, § 510(1), 113 Stat. 1445 (Nov. 12, 1999). The provision of the Gramm-Leach Bliley Act that authorizes administrative agencies to issue regulation interpreting the act became effective upon the act's enactment. Ibid., § 510(2).

[123] See 15 U.S.C.A. § 6803 (West 2000)

[124] See ibid., § 6802.

[125] Ibid., § 6802(c).

[126] Ibid., § 6805.

[127] See below for a discussion about the physician-patient privilege.

[128] See *Dillinbeck v. Hess*, 73 N.Y.2d at 284, 539 N.Y.S.2d at 711 (quoting *The Duchess of Kingston's Trial*, 20 How. St. Trials 355, 573 [1776]).

[129] See, e.g., N.Y. Pub. Health Law §§ 2803-c(1), (3)(f) (McKinney 1999) (patients' right to confidentiality in their personal and medical records in nursing homes and other facilities that provide "health related service[s]"), 2805-g(3) (confidentiality of hospital records), 4408(2)(e) (HMOs must have procedures to protect the confidentiality of medical records and other enrollee information); 10 N.Y.C.R.R. § 405.10(a)(6) (1999) (confidentiality of patients' hospital records and restriction on disclosure of the records

**The Physician-Patient Privilege**

The physician-patient privilege prohibits physicians and other health care providers from testifying in legal proceedings about patient information that relates directly to the patient's care and that the physician learns while caring for the patient.[130] The privilege also provides that individuals may not be forced to testify about communications with health care providers that took place while the individuals were obtaining treatment.[131]

The privilege does not prohibit individuals from being compelled to testify about "mere facts and incidents" of their medical histories.[132] For example, while the privilege would protect a patient with a heart condition from being compelled to testify about the content of discussions she had with her treating physician about the condition, it would not prevent the patient from being compelled to testify that she had the condition.[133]

Individuals who affirmatively place their physical or mental conditions at issue in litigation may not utilize the physician-patient privilege to prevent their opponents from obtaining information that is material to the litigation.[134] However, nonlitigants can utilize the privilege if they are asked to provide medical information about themselves.[135] This rule applies even when the individuals are related to the litigants and genetic information that is arguably relevant to the litigation is sought.

For example, in *Matter of New York County DES Litigation*,[136] the plaintiffs sued drug companies that manufactured diethylstilbestrol (DES) to recover for injuries they suffered because of their mothers' use of DES during pregnancy.[137] The drug companies sought to obtain the medical records of the plaintiffs' relatives in order to determine whether the plaintiffs' injuries were caused by genetic or hereditary factors rather than by DES.[138] Although the court permitted the defendants to obtain those portions of the mothers' medical histories that covered gestation, because these histories were inseparable from the plaintiffs' medical histories during that same period, the court ruled that the physician-patient privilege prevented the defendants from obtaining the

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only to "hospital staff involved in treating the patient[s] and individuals as permitted by Federal and State laws").

[130] See, e.g., N.Y. CPLR § 4504(a) (McKinney 1999); *Polsky v. Union Mut. Stock Life Ins. Co.*, 80 A.D.2d 777, 436 N.Y.S.2d 744 (N.Y. App. Div. 1981).

[131] See *Williams v. Roosevelt Hosp*., 66 N.Y.2d 391, 396, 497 N.Y.S.2d 348, 350 (1985).

[132] Ibid., 66 N.Y.2d at 396–97, 497 N.Y.S.2d at 350–351.

[133] See ibid.

[134] See *Dillenbeck v. Hess*, 73 N.Y.2d at 287, 539 N.Y.S.2d at 713; *Kaplowitz v. Borden, Inc.*, 189 A.D.2d 90, 594 N.Y.S.2d 744 (N.Y. App. Div. 1993) (because the plaintiff brought a lawsuit that put her genetic condition at issue, the physician-patient privilege did not prevent the disclosure of genetic information contained in her medical records).

[135] See *Matter of New York County DES Litig.*, 168 A.D.2d 44, 570 N.Y.S.2d 804 (N.Y. App. Div. 1991).

[136] 168 A.D.2d 44, 570 N.Y.S.2d 804 (N.Y. App. Div. 1991).

[137] Ibid., 168 A.D.2d at 45, 570 N.Y.S.2d at 804–805.

[138] Ibid., 168 A.D.2d at 45, 570 N.Y.S.2d at 805.

remainder of the mothers' records. The court also refused to order the plaintiffs' other relatives to disclose their medical records to the defendants, stating that, "The mere fact that a relative, distant or near in terms of kinship, has commenced a medical malpractice action alleging a birth defect should not subject all her relatives to the 'long arm' reach of the law authorizing their medical histories opened to all."[139]

Although there are many exceptions to the physician-patient privilege, such as the requirement that physicians report gunshot wounds to the police and the rule that patients may not assert the privilege to prevent physicians from testifying in child abuse hearings, the Court of Appeals has emphasized that "the physician-patient privilege is to be given a broad and liberal construction to carry out its policy."[140]

**Section 18 of the Public Health Law: Disclosure of Health Information by Health Care Providers**

Section 18 of the Public Health Law regulates the disclosure of individuals' health information by "health care providers" and by third parties who obtain "patient information" from "health care providers."[141] Section 18 includes within its coverage information obtained during "a health assessment for insurance and employment purposes."[142]

Subject to a number of exceptions,[143] Section 18 forbids health care providers from disclosing health information to third parties unless the subjects of the information have provided written authorization for the disclosure.[144] Any disclosure must be "limited to that information necessary in light of the reason for the disclosure."[145] Furthermore, Section 18 requires third parties to keep confidential all information that

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[139] Ibid., 168 A.D.2d at 46–48, 570 N.Y.S.2d at 805–06. The court ruled that the defendants could seek to obtain the relatives' records on an individual basis but that the relatives would be free to assert any privilege they felt was appropriate — including, apparently, the physician-patient privilege — to keep the records out of the defendants' hands. Ibid., 168 A.D.2d at 47–48, 570 N.Y.S.2d 806.

[140] *People v. Sinski*, 88 N.Y.2d 487, 492, 646 N.Y.S.2d 651, 653 (1996) (citations and internal quotations marks omitted).

[141] N.Y. Pub. Health Law § 18 (McKinney 1999).

[142] Ibid., § 18(1)(e).

[143] See ibid.

[144] See ibid., § 18(6); *Matter of Mantica v. New York State Department of Health*, 94 N.Y.2d 58, 62, 699 N.Y.S.2d 1, 4 (1999) ("The result that section 18(6) seeks to prevent is the disclosure of confidential medical records to third parties."); *Matter of Rabinowitz v. Hammons*, 228 A.D.2d 369, 369–370, 644 N.Y.S.2d 726, 726–727 (N.Y. App. Div. 1996) (disclosure of medical records to academic researcher forbidden under Section 18 because the subjects of the records had not provided written authorization for the disclosure).

[145] N.Y. Pub. Health Law § 18(6) (McKinney 1999).

health care providers disclose to them and mandates that all subsequent redisclosures of the information are governed by all of the disclosure rules contained in the statute.[146]

Persons who violate the provisions of Section 18 are subject to a fine and can be enjoined from continuing their illegal behavior.[147] Persons who *willfully* violate the provisions of Section 18 — that is, violate Section 18 knowing that their actions are illegal — can be charged with a misdemeanor, sentenced up to a year in prison, and fined up to $2,000.[148] Section 18 does not specifically give individuals the right to sue persons who violate its disclosure provisions, and it is unclear whether courts would infer a right to bring such lawsuits based on this section.[149]

Section 18 does not protect the confidentiality of health information that the subjects of the information reveal directly to persons or entities that are not "health care providers." For example, in *La Barge v. Haven of Schenectady, Inc.*,[150] the court ruled that Section 18 was not applicable to records of support group counseling sessions led by nonprofessional staff and volunteers in a not-for-profit corporation because the staff, the volunteers, and the corporation were not health care providers within the meaning of Section 18.[151]

### The Civil Rights and Insurance Laws: Confidentiality of Genetic Information

New York is one of a growing number of states that have enacted specific legislation protecting the confidentiality of genetic information. Section 79-l of the Civil Rights Law and Section 2612 of the Insurance Law regulate the disclosure of "genetic test" results. Section 79-l applies to everyone except insurers, and Section 2612 applies to insurers and persons who act on behalf of insurers.[152] Both statutes define a "genetic test" as "any laboratory test of human DNA, chromosomes, genes, or gene products to diagnose the presence of a genetic variation linked to a predisposition to a genetic disease

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[146] See ibid.; *Rockland County Patrolmen's Benevolent Ass'n, Inc. v. Collins*, 225 A.D.2d 534, 534, 638 N.Y.S.2d 747, 748 (N.Y. App. Div. 1996) (third parties violated Section 18 when they disclosed medical records to the New York State Retirement System without the subjects' authorizations).b

[147] See N.Y. Pub. Health Law §§ 12(1),(2), (5) (McKinney 1999).

[148] See ibid., § 12-b(2); *People v. Coe*, 71 N.Y.2d 852, 855, 527 N.Y.S.2d 741, 742 (1988).

[149] Compare *Mark G. v. Sabol*, 93 N.Y.2d 710, 718–722, 695 N.Y.S.2d 730, 733–735 (1999) (refusing to find an implied right of action for violation the Child Welfare Reform Act); *Carrier v. Salvation Army*, 88 N.Y.2d 298, 644 N.Y.S.2d 678 (1996) (find private right of action under New York Social Services Law § 460-d); *Larson v. Albany Med. Ctr.*, 252 A.D.2d 936, 936–938, 676 N.Y.S.2d 293, 294–295 (N.Y. App. Div. 1998) (refusing to infer a private right of action against hospital that allegedly violated N.Y. Civ. Rights Law § 79-i by discriminating against staff who refused to participate in abortions) with *Doe v. Roe*, 190 A.D.2d 463, 470–471, 599 N.Y.S.2d 350, 353–354 (N.Y. App. Div. 1993) (inferring a private right of action against persons who disclose HIV information in violation of Article 27-F of the Public Health Law).

[150] 170 Misc.2d 998, 652 N.Y.S.2d 498 (N.Y. Sup. Ct. 1996).

[151] Ibid., 170 Misc.2d at 998–1001, 652 N.Y.S.2d at 499–500.

[152] N.Y. Civ. Rights Law, § 79-l(6) (McKinney 1999); N.Y. Ins. Law § 2612(a) (McKinney 1999).

or disability in the individual or the individual's offspring."[153] The statutes specifically exclude from the definition of genetic test "any test of blood or other medically prescribed test in routine use that has been or may be hereafter found to be associated with a genetic variation, unless conducted purposely to identify such genetic variation."[154]

With limited exceptions, Sections 79-l and 2612 prohibit the performance of genetic tests on biological samples without the subject's prior written informed consent.[155] The informed consent form must include "the name of the person or categories of persons or organizations to whom the test results may be disclosed,"[156] as well as a statement that no tests other than those authorized will be conducted and that the sample will be destroyed within sixty days, unless the subject expressly authorizes a longer period of retention in writing.[157]

Absent a subject's additional informed consent, Sections 79-l and 2612 also prohibit the disclosure of genetic test results to any persons other than those listed on the informed consent document.[158] In addition, Section 79-l provides that, even if the subject consents to the disclosure of genetic test results to a health insurer or a health maintenance organization (HMO) because those results are "reasonably required" to process the subject's claim for coverage, the insurer or HMO may not redisclose that information internally beyond what is necessary to process the claim.[159] Furthermore, Section 79-l makes unlawful "unauthorized solicitation or possession" of genetic test results.[160]

Section 79-l exempts from its disclosure restrictions New York's newborn screening program, New York's program for genetically "fingerprinting" convicted criminals, and research on anonymous samples where an institutional review board (IRB) has approved the research protocol and has assured "the anonymity of the sources of the samples."[161] Also exempt is research (regardless of IRB approval) where the research subjects have provided a general waiver for the use of their samples for research, the

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[153] N.Y. Civ. Rights Law § 79-l(1)(a) (McKinney 1999); N.Y. Ins. Law § 2612(i) (McKinney 1999) ("the term genetic test shall have the same meaning as defined in section 79-l of the civil rights law"). The statutes also define genetic test as including "DNA profile analysis," but they do not define that term. Presumably, the term is meant to cover DNA tests for identification purposes.

[154] N.Y. Civ. Rights Law § 79-1(1)(a) (Mckinney 1999); N.Y. Ins. Law § 2612(i) (McKinney 1999).

[155] N.Y. Civ. Rights Law § 79-l(2) (McKinney 1999); N.Y. Ins. Law § 2612(a) (McKinney 1999).

[156] N.Y. Civ. Rights Law § 79-l(2)(b)(6) (McKinney 1999); N.Y. Ins. Law § 2612(b)(6) (McKinney 1999).

[157] N.Y. Civ. Rights Law § 79-l(2)(b)(7) (McKinney 1999); N.Y. Ins. Law § 2612(b)(7) (McKinney 1999).

[158] N.Y. Civ. Rights Law § 79-l(2)(d) (McKinney 1999); N.Y. Ins. Law § 2612(d) (McKinney 1999). For further discussion of the informed consent requirements of Sections 79-l and 2612, see Chapter 7, page 183.

[159] N.Y. Civ. Rights Law § 79-l(3)(a) (McKinney 1999).

[160] Ibid.

[161] Ibid., §§ 79-l(4)(a), 79-l(4)(b), 79-l(4)(c), 79-l(7).

researchers remove all of the sample identifiers, and the research results cannot be linked to the subjects.[162] In addition, Section 79-l permits courts to order the disclosure of genetic test results without the informed consent of the subject.[163] However, before issuing such an order, the court must "consider the privacy interests of the individual subject of the genetic test and of close relatives of such individual, the public interest, and, in the case of medical or anthropological research, the ethical appropriateness of the research."[164]

Willful violators of Section 79-1's disclosure provisions can be charged with a misdemeanor, imprisoned up to ninety days, and fined up to $5,000.[165] Nonwillful violators can be convicted of a violation and fined up to $1,000.[166] Violators of Section 2612's disclosure provisions can be convicted of a misdemeanor, fined up to $5,000, and subject to cease and desist orders by the Superintendent of Insurance.[167] Outside of certain fines and other sanctions that can be levied by the Superintendent of Insurance, individuals and organizations must be proven guilty beyond a reasonable doubt before they may be convicted of a misdemeanor or violation and fined.[168] In addition, Sections 79-1 and 2612 do not explicitly authorize private lawsuits against parties who violate their informed consent provisions, and it is unclear whether courts would infer a right to bring such lawsuits.[169]

**New York Common Law**

New York courts have ruled as a matter of common law that physicians have a fiduciary duty not to disclose their patients' confidential information without the patients' consent. Physicians who violate that duty are subject to liability for their patients' economic losses, mental distress, consequential damages, and punitive damages.[170]

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[162] Ibid. §§ 79-l(2)(c), 79-l(9).
[163] Ibid., §§ 79-l(4)(c), 79-l(4)(d).
[164] Ibid., § 79-l(4)(d).
[165] Ibid., § 79-l(5)(b).
[166] Ibid., § 79-l(5)(a).
[167] N.Y. Ins. Law §§ 2612(j), 109(a), 2406(a), 2406(d) (McKinney 1999).
[168] See N.Y. Penal Law §§ 10.00(3), 55.10 (McKinney 1999); N.Y. Crim. Proc. Law § 70.20 (McKinney 1999).
[169] See note 149, above.
[170] See, e.g., *Tighe v. Ginsberg*, 146 A.D.2d 268, 270–272, 540 N.Y.S.2d 99, 99–101 (N.Y. App. Div. 1989); *MacDonald v. Clinger*, 84 A.D.2d 482, 483–487, 446 N.Y.S.2d 801, 802–805 (N.Y. App. Div. 1982); *Doe v. Roe*, 42 A.D.2d 559, 560, 345 N.Y.S.2d 560, 561–62 (N.Y. App. Div.), *aff'd*, 33 N.Y.2d 902, 902–904, 352 N.Y.S.2d 626, 626 (1973). Cf. *Harley v. Druzba*, 169 A.D.2d 1001, 1001–1002, 565 N.Y.S.2d 278, 279–280 (N.Y. App. Div. 1991) (patient can sue social worker for breach of fiduciary duty of confidentiality); *Oringer v. Rotkin*, 162 A.D.2d 113, 113–114, 556 N.Y.S.2d 67, 68 (N.Y. App. Div. 1990) (patient can sue psychologist for breach of fiduciary duty of confidentiality).

## Waivers of Confidentiality

Waiver, in the legal context, is "an intentional relinquishment or abandonment of a known right or privilege."[171] Commentators have pointed out that confidentiality protections are of limited value if they can easily be waived.[172]

Currently, insurance companies regularly require applicants to waive their rights to health and genetic information confidentiality as a condition of coverage, and applicants "routinely" comply.[173] One commentator has questioned the appropriateness of this "coerced disclosure,"[174] although courts have held that such waivers are necessary to prevent fraud by insurance applicants.[175] Furthermore, health insurers ordinarily will not pay for medical treatments unless the covered patients waive their rights to confidentiality of their medical records.[176] As a result, individuals sometimes pay for medical treatment out of pocket rather than reveal that they have sought care.[177]

New York courts have held that individuals can waive their rights to the physician-patient privilege, although such waivers are strictly construed.[178] Furthermore, while in most cases the Civil Rights Law and the Insurance Law prohibit the use of general waivers to nullify the requirement of obtaining informed consent to genetic

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[171] *Doe v. Marsh*, 105 F.3d 106, 111 (2d Cir. 1997) (quoting *Johnson v. Zerbst*, 304 U.S. 458, 464, 58 S. Ct. 1019, 1023 (1938)).

[172] A. Caplan, "Ethics on the Genetic Frontier," presentation at the American Association for the Advancement of Science annual meeting, Philadelphia, PA, February 12–17, 1998.

[173] J. V. Jacobi, "The Ends of Health Insurance," *University of California at Davis Law Review* 30 (1997): 311, 320 n.34. See also M. A. Rothstein, "Genetic Privacy and Confidentiality: Why Are They So Hard to Protect," *Journal of Law, Medicine, and Ethics* 26 (1998): 198, 198 ("If a third party has enough leverage and economic power, it can go to an individual and require him/her to execute a release that authorizes a physician to release the medical records to a third party.").

[174] Ibid.

[175] See R. A. Wade, "The Ohio Physician-Patient Privilege: Modified, Revised, and Defined," *Ohio State Law Journal* 49 (1989): 1147, 1154 n.56.

[176] See *Henry v. Lewis*, 102 A.D.2d 430, 435, 478 N.Y.S.2d 263, 268 (N.Y. App. Div. 1984); New York State Legislative Commission on Science and Technology, *DNA-Based Tests: Policy Implications for New York State* (Albany, NY: Legislative Commission on Science and Technology, 1994), 37–38.

[177] See, e.g., L. Eustace-McMillan, "Protecting Private Medical Information: Liability for Unauthorized Disclosure," University of Houston Law Center, Houston, TX, website: *http://www.law.uh.edu/healthlawperspectives/Privacy/991217Protecting.html*, visited December 29, 1999; R. M. Gellman, "Proscribing Privacy: The Uncertain Role of the Physician in the Protection of Patient Privacy," *North Carolina Law Review* 62 (1984): 255, 259 n.14 (citing estimate that up to 15 percent of employees who seek mental health care and have mental health care benefits pay for their care out of their own pockets because they do not want their employers to know that they are seeking such care).

[178] *Henry v. Lewis*, 102 A.D.2d at 435, 478 N.Y.S.2d at 268. New York courts also have held that "an authorization to release medical information to a specific party does not constitute a waiver of the physician-patient privilege as far as other parties are concerned." Ibid.

testing,[179] they do not specifically prohibit general waivers of the statutes' restrictions on disclosure of genetic test results. Similarly, Section 18 of the Public Health Law prohibits waivers of some of it provisions[180] but nowhere states that waivers of its disclosure provisions are void.

In at least one circumstance, the New York Court of Appeals refused to recognize waivers of health information confidentiality protections,[181] although it did not fully explain the criteria for deciding when such waivers are ineffective.

## Disclosure of Genetic Information to Family Members

Under the common law, when a patient has a highly communicable disease, such as typhus, the patient's physician has a duty to warn members of the patient's household about the disease and to instruct them about how to avoid contracting it.[182] New York regulations contain similar requirements.[183] In addition, the New York Public Health Law mandates that physicians report cases of HIV infection and AIDS to the state health department,[184] and that, in appropriate cases, the state or local health department or the physicians inform the patient's contacts about their possible exposure to HIV.[185]

These and other exceptions to physician-patient confidentiality reflect society's judgment that, in certain situations, an individual's right to confidentiality must bow to other important societal interests. Few courts have ruled, however, on whether physicians or other health care providers who learn that their patients have genetic mutations that indicate a predisposition to disease may or must warn the patients' family members that they also may have similar mutations.

Most commentators agree that health care providers have an ethical obligation to urge their patients to share "important genetic information" with their families.[186] Yet,

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[179] N.Y. Civ. Rights Law § 79-l(2)(c) (McKinney 1999); N.Y. Ins. Law § 2612(c) (McKinney 1999).

[180] See N.Y. Pub. Health Law § 18(9) (McKinney 1999).

[181] See *Matter of Grattan v. People*, 65 N.Y.2d 243, 245–246, 491 N.Y.S.2d 125, 127–128 (1985) (individual who participated in a sexually transmitted disease program was unable to waive the program's statutory confidentiality provisions because allowing such waivers would undercut the public's trust and participation in the program).

[182] See, e.g., *Tenuto v. Lederle Lab.*, 90 N.Y.2d 606, 611–614, 665 N.Y.S.2d 17, 19–21 (1997).

[183] See, e.g., 10 N.Y.C.R.R. § 2.27 (1998) (requiring physicians who diagnose highly communicable diseases in their patients to "advise other members of the [patient's] household regarding precautions to be taken to prevent further spread of the disease"); New York State Public Health Council, *Safeguarding the Confidentiality of Health Information*, 19–20.

[184] N.Y. Pub. Health Law § 2130(1) (McKinney 1999).

[185] Ibid., §§ 2131, 2133, 2782(4) (McKinney 1999). A contact is "an identified spouse or sex partner of the [patient], a person identified as having shared hypodermic needles or syringes with the [patient] or a person who the [patient] may have exposed to HIV under circumstances that present a risk of transmission of HIV, as determined by the commissioner." Ibid., § 2780 (10).

[186] Annas, Glantz, and Roche, "The Genetic Privacy Act," 158. Accord, e.g., J. E. Merz, M. K. Cho, and P. Sankar, "Familial Disclosure in Defiance of Nonconsent," *American Journal of Human Genetics* 63 (1998):

some of these commentators also argue that providers should be prohibited from disclosing this information directly to family members without the patient's consent. These commentators maintain that most patients will inform their families themselves, that family members are free to seek genetic testing or counseling on their own, and that it would be difficult to set "logical boundaries" to a privilege or duty to disclose patients' genetic information to family members.[187]

In *Pate v. Threlkel,*[188] the Florida Supreme Court adopted at least some of this reasoning. In *Pate*, the plaintiff, who suffered from an advanced form of hereditary cancer, sued a physician who had treated the plaintiff's mother for the disease a number of years earlier but who had allegedly not warned the plaintiff or her mother that the plaintiff should be tested for the disease.[189] The court ruled that, even if a physician has a duty to warn a third party about a genetically transferable disease, "that duty will be satisfied by warning the patient."[190] The court based its decision on laws that prohibit physicians from disclosing health information without patient consent. It also reasoned that "the patient can ordinarily be expected to pass on the warning" and that requiring physicians to "seek out and warn various members of the patient's family would often be difficult or impractical and would place too heavy a burden on the physician."[191]

Some commentators maintain, by contrast, that if patients refuse to disclose relevant genetic information to at-risk family members, health care providers should have the right or privilege to disclose the information themselves.[192] The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research contends that because "the decision to breach professional confidentiality is such a weighty one, it may also be advisable to seek review by an

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898, 899; S. M. Suter, "Whose Genes Are These Anyway? Familial Conflicts over Access to Genetic Information," *Michigan Law Review* 91 (1993): 1854, 1883–1884.

[187] Merz, Cho, and Sankar, "Familial Disclosure in Defiance of Nonconsent," 898–899; Annas, Glantz, and Roche, "The Genetic Privacy Act," 158. But see S. Ain, "Fear of Tay-Sachs Resurgence Seen," *The Jewish Week*, December 11, 1998, The Jewish Week website: *http://www.thejewishweek.com/jwcurr.exe?9812118*, visited December 16, 1998 (discussing the "surpis[ing] number of couples" who are Tay-Sachs carriers and refuse to tell their relatives that they may be carriers as well).

[188] 661 So.2d 278 (Fla. 1995).

[189] Ibid., at 279.

[190] Ibid., at 282.

[191] Ibid. The court sent the case back to the lower court for further proceedings.

[192] Suter, "Whose Genes Are These Anyway?" 1883–1884; President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions* (Washington, D.C.: President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, 1983), 44–45; American Society of Human Genetics, "Professional Disclosure of Familial Genetic Information," *American Journal of Human Genetics* 62 (1998): 474, 474, 482.

appropriate third party."[193] The recognition of a privilege for health care providers to disclose relevant genetic information to at-risk family members would not *require* them to do so. Rather, under appropriate circumstances, it would immunize health care providers from liability for violating confidentiality laws.[194]

The American Society of Human Genetics has adopted this view. It maintains that "disclosure should be permissible where attempts to encourage disclosure on the part of the patient have failed; where the harm is highly likely to occur and is serious and foreseeable; where the at-risk relative is identifiable; . . . where either the disease is preventable/treatable or medically accepted standards indicate that early monitoring will reduce the genetic risk;" and "where the harm that may result from failure to disclose outweighs the harm that may result from the disclosure."[195] A number of government and other panels that have studied this issue have adopted similar positions.[196]

Stressing the "impact on society" of the "human suffering and economic burden" caused by genetic diseases, at least one commentator maintains that health care professionals have a *duty* to disclose their patients' genetic status to family members when the family members will suffer "serious" harm without the disclosure.[197] A New Jersey Appellate court echoed at least some of this reasoning in *Safer v. Estate of Pack.*[198] In *Safer*, the plaintiff, who suffered from colon cancer, sued a physician who had treated her father for the same hereditary condition but had failed to warn the plaintiff or her mother about its hereditary nature or that the plaintiff should be monitored for signs of the disease.[199] The court ruled that a physician's duty to warn third parties "known to be at risk of avoidable harm from a genetically transmissible condition" was the same as the duty to warn third parties at risk of contracting contagious diseases.[200] The court pointed out that, as in the infectious disease context, "the individual or group at risk is easily identified, and that substantial future harm may be averted or minimized by a timely and effective warning."[201] Specifically disagreeing with the reasoning in *Pate*, the *Safer* court ruled that a physician's duty to warn third parties of a possible "genetic threat" will not always be satisfied by urging patients to inform their families themselves.[202]

For over twenty years, New York courts have recognized malpractice lawsuits against physicians for failing to give proper genetic advice to parents in the reproductive

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[193] President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions*, 44–45.
[194] See Suter, "Whose Genes Are These Anyway?" 1877–1884.
[195] American Society of Human Genetics, "Professional Disclosure," 474.
[196] See e.g., ibid., 478 and n.9.
[197] J. A. Kobrin, "Medical Privacy Issue: Confidentiality of Genetic Information," *U.C.L.A. Law Review* 30 (1983): 1283, 1312–1315.
[198] 291 N.J. Super. 619, 677 A.2d 1188 (N.J. Super. Ct. App. Div. 1996).
[199] Ibid., 291 N.J. Super at 621–623, 677 A.2d at 1189–1190.
[200] Ibid., 291 N.J. Super. at 625–626, 677 A.2d at 1191–1192.
[201] Ibid., 291 N.J. Super. at 626, 677 A.2d at 1192.
[202] Ibid., 291 N.J. Super. at 625, 627, 677 A.2d at 1191–1193.

context.[203] However, New York courts have not discussed whether physicians have a duty to warn patients or their relatives that the relatives may have the same genetic mutations as the patients. Currently, the New York Civil Rights law prohibits health care providers from disclosing a patient's genetic information to the patient's family members, unless the patient specifically consents to the disclosure or the health care providers obtain a court order authorizing the disclosure.[204] Before a court may issue an order compelling disclosure, it must consider "the privacy interests of the individual subject of the genetic test and of close relatives of such individual," as well as "the public interest."[205]

## Anonymous Genetic Testing

Some commentators have recommended that, to encourage individuals to take genetic tests and to prevent unconsented-to acquisition of genetic information by insurers, employers, and others, patients should be permitted to take certain types of genetic tests without revealing their identities to the health care providers administering the tests.[206] These commentators recognize that anonymous testing would generally only be appropriate when the test results will be meaningful without having to test the patient's family members. They also caution against the use of anonymous testing in situations where treatment might be available to those who test positive.[207] In general, the commentators maintain that anonymous testing would be most appropriate for "largely untreatable" single gene disorders for which an accurate genetic test is available.[208]

Other commentators believe that anonymous genetic testing is generally inappropriate.[209] Some contend that in order to provide proper pretest counseling to

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[203] See, e.g., *Martinez v. Long Island Jewish Hillside Medical Center*, 70 N.Y.2d 697, 518 N.Y.S.2d 955 (1987); *Becker v. Schwartz*, 46 N.Y.2d 401, 413 N.Y.S.2d 895 (1978). See also *Jorge v. New York City Health and Hospitals Corp.*, 79 N.Y.2d 905, 581 N.Y.S.2d 654 (1992) (dismissing as time-barred a lawsuit by the father of child born with sickle cell disease against a hospital that misread the father's sickle cell test during his wife's pregnancy); *Weed v. Meyers*, 251 A.D.2d 1062, 674 N.Y.S.2d 242 (N.Y. App. Div. 1998) (dismissing lawsuit against physician for failing to warn father that his future children could inherit his retinoblastoma condition).

[204] See pages 260–261, this chapter.

[205] N.Y. Civil Rights Law § 79-l(3)(d) (McKinney 1999).

[206] See M. J. Mehlman et al., "The Need for Anonymous Genetic Counseling and Testing," *American Journal of Human Genetics* 58 (1996): 393, 393–397. This is to be distinguished from genetic testing where health care providers know the patient's identity, but send the patient's biological sample to a laboratory identified only by a code. There appears to be no dispute that this practice is acceptable.

[207] Ibid.

[208] Ibid., 395.

[209] See M. M. Burgess et al., "Dilemmas of Anonymous Predictive Testing for Huntington Disease: Privacy vs. Optimal Care," *American Journal of Medical Genetics* 71 (1997): 197; W. R. Uhlman et al., "Questioning the Need for Anonymous Genetic Counseling and Testing," *American Journal of Human*

patients and to determine the proper tests to perform, health care providers need accurate family history information that can be truly verified only through access to family medical records. They claim that it would be burdensome to have to anonymize these records in order to maintain the anonymity of the patient and that to do so would increase the possibility of clinical errors.[210]

Still others argue that anonymous genetic testing would likely have a deleterious effect on genetic counseling.[211] They point out that genetic counseling usually entails psychological assessment of the patient as well an assessment of the patient's social support network; a patient's anonymity can interfere with these assessments.[212] In addition, these commentators contend that anonymous genetic testing can also interfere with the development of a personal relationship and rapport between the patient and the genetic counselor, as well as proper counseling and follow-up that are important for the counseling to effective.[213] These commentators recommend that (1) the appropriateness of offering anonymous testing should be evaluated on a case-by-case basis and should include an a psychosocial analysis of the patient, (2) anonymous testing should be performed only as part of a research protocol because "it appears to reduce the safeguards present in most predictive testing programs," (3) anonymous testing should not be performed if the patient has "a complicated psychosocial history," and (4) patients should be told that anonymous testing does not guarantee that they will not lose insurance coverage.[214]

Commentators have pointed out that patients who withhold the results of anonymous genetic tests from insurance companies when applying for insurance may be committing fraud and could lose their insurance benefits should the insurance companies learn about the tests.[215] In New York, if an individual makes a fraudulent and material misrepresentation on an insurance application, the individual's insurer can, in many circumstances, rescind insurance coverage.[216]

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*Genetics* 59 (1996): 968 (letter); E. W. Clayton and M. A. Rothstein, "Anonymous Genetic Testing: Reply to Mehlman et al.," *American Journal of Human Genetics* 59 (1996): 1169 (letter).

[210] Uhlman et al., "Questioning the Need for Anonymous Genetic Counseling and Testing," 969.

[211] Burgess et al., "Dilemmas of Anonymous Predictive Testing," 198, 200.

[212] Ibid., 199.

[213] Ibid., 198, 200.

[214] Ibid., 200.

[215] Ibid., 200; Clayton and Rothstein, "Anonymous Genetic Testing: Reply to Mehlman et al.," 1169. See generally J. S. Blumenkopf and B. A. Friedman, "The Material Misrepresentation Defense," *Winter Brief* 27 (American Bar Association, 1998): 59 (discussing the circumstances under which insurance companies can refuse to pay insurance benefits if insureds have made material misrepresentations or omissions on insurance applications).

[216] See N.Y. Ins. Law §§ 3105, 3216(d)(1)(B) (McKinney 1999); *New England Mut. Life Ins. Co. v. Doe*, 93 N.Y.2d 122, 131, 688 N.Y.S.2d 459, 463 (1999); *Aguilar v. United States Life Insurance Co.*, 162 A.D.2d 209, 556 N.Y.S.2d 584 (N.Y. App. Div. 1990). However, if a life insurance company fails to attempt to rescind an insurance policy within two years of its issuance, it may be prohibited from doing so regardless of whether the insured made fraudulent representations. See N.Y. Ins. Law §§ 3203, 3220 (McKinney 1999); *Gerhardt v. First Reliance Standard Life Ins. Co.*, 1994 WL 38678 *1 (S.D.N.Y. 1994).

## Certificates of Confidentiality

In response to concerns that individuals may refrain from participating in genetic research projects out of fear that the results could be obtained by insurers, employers, or others, some commentators have advocated that genetic researchers acquire certificates of confidentiality for their projects.[217] Certificates of confidentiality are documents issued by the Secretary of the Department of Health and Human Services that prevent researchers from being compelled to disclose identifying information about research subjects in civil, criminal, legislative, administrative, and other proceedings.[218] For example, in *People v. Newman*,[219] the New York Court of Appeals ruled that a methadone maintenance program that had a certificate of confidentiality did not have to comply with a subpoena, issued as part of a murder investigation, that demanded patient photographs.[220] The confidentiality protections of the certificates are meant to encourage individuals to participate in research whose results have the potential to cause the research subjects "adverse economic, psychological, and social consequences," including social stigmatization, employment discrimination, and adverse insurance decisions.[221]

Among the types of research projects the Secretary has indicated are sufficiently "sensitive" to be eligible for certificate of confidentiality protection are projects involving

"genetic information."[222] The National Cancer Institute, which is part of the National Institutes of Health, has specified that projects involving genetic testing for cancer predisposition are eligible for such certificates.[223]

Notwithstanding the above, certificates of confidentiality are difficult to obtain, both because the process for obtaining a certificate is lengthy and arduous and because the Secretary issues such certificates "sparingly."[224] In addition, certificates of

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[217] See, e.g., C. L. Earley and L. C. Strong, "Certificates of Confidentiality: A Valuable Tool for Protecting Genetic Data," *American Journal of Human Genetics* 57 (1995): 727.

[218] 42 U.S.C.A. § 241(d) (West 1999); National Cancer Institute, *Certificates of Confidentiality: Background Information and Application Procedures*, National Cancer Institute website: *http://cancertrials.nci.nih.gov/NCI_CANCER_TRIALS/zones/TrialInfo/Resources/conf/certconf.pdf*, visited December 7, 1999, 1; National Institutes of Health, "Privacy Protection for Research Subjects 'Certificates of Confidentiality,'" National Institutes of Health website: *http://grants.nih.gov/grants/oprr/humansubjects/guidance/certconpriv.htm*, visited December 7, 1999.

[219] 32 N.Y.2d 379, 345 N.Y.S.2d 502 (1973).

[220] Ibid.

[221] National Cancer Institute, *Certificates of Confidentiality*, 5.

[222] National Institutes of Health, "Privacy Protection for Research Subjects 'Certificates of Confidentiality.'" National Institutes of Health website: *http://grants.nih.gov/grants/oprr/humansubjects/guidance/certconpriv.htm*.

[223] National Cancer Institute, *Certificates of Confidentiality*, 5.

[224] Ellen Wright Clayton, "Informed Consent and Genetic Research," in *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*, ed. Mark A. Rothstein (New Haven, CT: Yale University Press,

confidentiality neither prohibit researchers from voluntarily disclosing identifying information about their research subjects nor prevent research subjects from revealing such information themselves.[225] Thus, even if an individual has participated in a genetic research project that was covered by a certificate of confidentiality, an insurer — absent other legal prohibitions — could still require individuals to reveal their individual results from those projects as a condition of obtaining insurance.[226]

## Conclusions and Recommendations

### Level of Confidentiality Protections for Genetic Information and Other Medical Information

**All personal medical information, including genetic information, should receive a uniform, high level of confidentiality protection. Absent new, comprehensive federal legislation or regulation that provides such protection, New York should enact comprehensive medical confidentiality legislation that does so.**

The improper disclosure of medical information can have negative effects on individuals and their families, including discrimination, stigma, and family perturbations. It also can lead to an erosion of trust between patients and health care providers, which can interfere with the provision of appropriate health care. The sensitivity of medical information does not depend on whether it relates to genetic or nongenetic matters. Just as disclosure of genetic information can be harmful, the same can be true for the disclosure of, for example, psychiatric information or information about infectious diseases.

In addition to being ethically problematic, creating different levels of confidentiality protections for different types of medical information makes record-keeping difficult, time-consuming, and expensive. Moreover, these differential protections can inadvertently result in disclosure of the very information whose confidentiality is sought to be protected. For example, when responding to requests for patient records that happen to contain HIV-related information, some custodians of records in New York State have reportedly stated that they cannot disclose the complete records because they are prohibited by statute from doing so. Because HIV-related information is one of the few types of medical information in New York that receives

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1997), 129; National Cancer Institute, *Certificates of Confidentiality*, 3; Telephone interview with Olga Boikess, Senior Advisor to the Executive Officer of Resource Management, National Institutes of Mental Health, October 30, 1998.

[225] Clayton, "Informed Consent and Genetic Research," 130; National Cancer Institute, *Certificates of Confidentiality*, 3–4; National Institutes of Health, "Privacy Protection for Research Subjects 'Certificates of Confidentiality.'"

[226] See Clayton, "Informed Consent and Genetic Research," 130. For a discussion of the use of genetic information by insurers, see Chapter 10.

heightened confidentiality protections, this response creates a red flag that the patient's record likely includes information about HIV.

Accordingly, we believe that all medical information should receive a uniform, high level of confidentiality protection. Because current statutory and common law rules for medical information confidentiality do not provide such protections, there is a need for legislative or regulatory reform. Unless the federal government enacts such protections in the near future, New York State should do so. Moreover, as the Special Committee on Medical Information Confidentiality of the New York State Public Health Council concluded, even if the federal government enacts comprehensive medical confidentiality protections, New York State should enact additional protections, to the extent permissible under federal law, if the federal protections are found to be lacking.

### Recommendations for Amending New York's Genetic Confidentiality Laws If Comprehensive Confidentiality Protections Are Not Enacted

Although we advocate the enactment of comprehensive confidentiality protections for all medical information, we recognize the enormous complexity of the issues involved. Because the focus of our report is genetic information, and because New York has already enacted statutes concerning the confidentiality of such information, we address below several legislative issues that will require attention if comprehensive confidentiality protections are not enacted. In making these recommendations, we do not intend to signal a retreat from our position that enacting comprehensive medical information confidentiality protections should be an important priority both in New York State and nationally.

#### *Confidentiality Protections for Genetic Information*

**Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to protect the confidentiality of all genetic information.**

As currently written, New York's genetic confidentiality statutes protect the confidentiality of the results of laboratory genetic tests that reveal genetic information associated with future disease in oneself or one's offspring. However, such genetic information also can be revealed in other ways. For example, having a child with cystic fibrosis indicates that an individual is a carrier for that disease, even if the individual never undergoes genetic tests. If the individual's carrier status is noted in the medical record, the information will be as sensitive as if it had been determined through DNA

testing. Because the way in which genetic information is learned is not relevant to the confidentiality protections it should be accorded, New York's genetic confidentiality statutes should protect the confidentiality of genetic information regardless of how it is determined.

Although our report focuses primarily on genetic information that is associated with future disease risk in oneself or one's offspring, we believe that the confidentiality concerns that apply to such information also apply to other genetic information. For example, employers who wish to limit the cost of the health benefits they provide to their employees might discriminate against individuals based on their genetic information if the individuals exhibit symptoms of the disease associated with that information.[227] Employers might also discriminate against individuals whose pharmacogenetic information reveals that they would require expensive medications if they were to become ill. Similarly, employers might use environmental susceptibility information to exclude individuals from particular jobs when it is inappropriate to do so.[228] Accordingly, New York's genetic confidentiality statutes should be amended to protect the confidentiality of all genetic information.

***Confidentiality Protections for the Use of Genetic Services***

**Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to protect the confidentiality of the fact that an individual has obtained and/or inquired about genetic testing and/or counseling. The statutes also should be amended to protect the confidentiality of the content of the inquiries and/or counseling.**

For a variety of reasons, people who inquire about or obtain genetic testing or counseling may want to keep the fact that they have done so and the content of the inquiries or counseling confidential. These can include fears of employment and insurance discrimination, the desire to determine their genetic status without alarming family members, or simply a desire for privacy. Concerns about unconsented-to disclosures of the content of genetic counseling sessions or the fact that individuals have inquired about or obtained genetic testing or counseling may lead some people to avoid seeking potentially beneficial genetic services.

New York's genetic confidentiality statutes currently protect neither the confidentiality of the fact that individuals have inquired about or obtained genetic testing or counseling nor the confidentiality of the content of the inquiries or counseling. We

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[227] As currently written, New York's genetic confidentiality statutes do not protect the confidentiality of genetic information if the subject of the information exhibits or has exhibited symptoms of the disease associated with that information. See, e.g., N.Y. Civ. Rights Law § 79-l(1)(b) (McKinney 1999).

[228] A discussion of the circumstances under which it might be appropriate for employers to utilize environmental susceptibility information in making employment decisions is beyond the scope of this report.

recommend that the statutes be amended to protect the confidentiality of all of this information.

***Scope of Consented-to Disclosure of Genetic Information by Persons Other Than the Subject of the Information***

**Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to limit the disclosure of genetic information by persons other than the subject of the information to the amount necessary in light of the reason for the disclosure. The statutes also should be amended to limit such disclosures to those persons who have a need for the information in light of the reason for the disclosures.**

New York law currently provides that disclosure of a patient's medical information by health-care providers requires the patient's consent and that all subsequent redisclosures of that information by third parties also require the patient's consent. Moreover, the disclosures must be limited to the amount of information necessary in light of the purpose of the disclosure. Because genetic information is a type of medical information, this law applies to genetic information as well.

In addition to genetic information originally disclosed to third parties by health care providers, New York's genetic testing laws prohibit the disclosure of genetic information by anyone, absent patient consent, regardless of how the person came into possession of the information. However, New York's genetic confidentiality laws do not limit consensual disclosures to the amount of information necessary in light of the purpose of the disclosure. Thus, if an individual reveals his or her genetic information to a third party directly — for example, to an insurance company — and then authorizes the insurance company to redisclose the information to someone else, there are no additional checks on the disclosure of the information by the insurance company. We believe that New York's genetic confidentiality statutes should be amended to close this loophole. The laws should require that consent-to disclosure forms specify the purpose of the disclosure and that any disclosure should be limited to the amount of information necessary in light of the specified purpose.

When an individual consents to the disclosure of genetic information to an organization, the consent should not operate carte blanche for all persons associated with the organization to have access to it. Instead, access should be limited to persons who have a need for the information in light of the reason for the disclosure. For example, if an individual consents to the disclosure of genetic information to insurance companies for reimbursement purposes, only insurance company employees who are involved in the

reimbursement process should have access to the information, not everyone who works for the company.

***Permissible Third-Party Disclosures of Disease-Associated Genetic Information without the Subject's Consent***

**Assuming that comprehensive medical confidentiality protections are not adopted, the legislature should review and, if appropriate, amend the genetic confidentiality statutes in light of the recommendations of the Special Committee on Medical Information Confidentiality of the New York State Public Health Council about legitimate disclosures of medical information without patient consent.**

New York's genetic confidentiality statutes appear to prohibit unconsented-to third-party disclosures of genetic information even in circumstances where such disclosures might be appropriate. For example, read literally, the statutes might prohibit access by health accreditation and oversight review organizations to genetic information contained in medical records without the specific consent of the subject of those records. In addition, the statutes even could be interpreted to prohibit patients from disclosing relevant genetic information about their blood relatives to physicians as part of a medical history, unless they obtain their relatives' written consent. The Special Committee on Medical Information Confidentiality of the New York State Public Health Council has recommended circumstances under which individually identifiable health information may be disclosed without patient consent.[229] We recommend that the legislature thoroughly review the Special Committee's recommendations and amend New York's genetic confidentiality legislation to allow unconsented-to disclosures of genetic information where necessary and appropriate.

***Waivers of Genetic Confidentiality Protections***

**Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to render nonwaivable all of the confidentiality rights they provide.**

Confidentiality protections are of limited utility if individuals can, as a practical matter, be compelled to waive them. For example, insurance companies that wish to share their insureds' medical information with other insurers could make waivers of the genetic confidentiality protections a condition of receiving coverage or reimbursement. Because individuals seeking insurance have far less bargaining power than insurers, they will have virtually no choice but to comply with such demands. The only effective way to achieve the societal goal of genetic information confidentiality, therefore, is to render

[229] A list of these recommendations is contained in Appendix A, page 397.

such waivers unenforceable, just as the law already renders unenforceable the waiver of other important consumer rights.[230]

Making the genetic confidentiality protections nonwaivable would not preclude necessary disclosure of genetic information by third parties; it would mean only that such disclosures would have to conform with the procedures set forth in the statutes.

***Disclosure of Genetic Information to Relatives***

**Health care providers should discuss with their patients the medical ramifications of the patient's genetic information for the patient's relatives. Health care providers should encourage their patients to disclose genetic information to relatives when the disclosure is likely to help the relatives avert or treat disease or to make reproductive decisions. Health care providers should not disclose their patient's genetic information to the patient's relatives without the patient's consent or a court order. Courts should be authorized to permit health care providers to make such disclosures only when where (1) the patient refuses to disclose the information to an identified relative despite attempts by the health care provider to convince him or her to do so; (2) without disclosure, serious harm to the relative is highly likely to occur; (3) with disclosure, the harm can be averted or its chances of occurring significantly minimized; and (4) the harm that may result from failure to disclose outweighs the harm that may result from the disclosure.**

An individual's genetic information can have medical ramifications for the individual's relatives. Health care providers should discuss these ramifications with their patients, and they should encourage their patients to disclose genetic information to relatives when such disclosures are likely to help the relatives avert or treat disease or make reproductive decisions. For example, because preventive treatments are available, health care providers should urge patients who have inherited an APC gene mutation that genetically predisposes the patients to familial colon cancer[231] to warn their relatives that they may have the same genetic predisposition. When disclosure of a patient's genetic information will not help the patient's relatives treat or avert disease and will not aid the relatives in making reproductive decisions, providers should generally not encourage

[230] For example, the Public Health Law renders void all waivers of an individuals' rights to inspect, copy, or seek correction of information in their medical records. See N.Y. Pub. Health Law § 18(9) (McKinney 1999). Other nonwaivable consumer rights include the warranty of habitability for residential leases, N.Y. Real Prop. Law § 235-b(2) (McKinney 1999), the obligation to perform a contract in good faith, N.Y. U.C.C. § 1-102(3) (McKinney 1999), and the right to rescind purchases made through door-to-door sales, 16 C.F.R. § 429 (1998).

[231] APC stands for adenomatous polyposis coli; see Chapter 2, page 38.

disclosure, since the relatives might not want to learn about genetic predispositions when there is nothing they can do about them.

In general, health care providers should not disclose a patient's genetic information to the patient's relatives without the patient's consent. The possibility of such unconsented-to disclosures might make patients worry about the confidentiality of all private medical information, which could undermine the trust on which the relationship between health-care providers and patients rests. This in turn could endanger patient health by causing patients to withhold relevant information or decline to seek genetic testing altogether, even when such testing might provide them with important health benefits.

The number of cases in which family members have a genuine medical interest in the results of a patient's genetic tests — that is, situations where test results might help family members prevent or treat diseases that otherwise would be likely to cause serious harm — is relatively small, at least for now. In the overwhelming majority of these cases, we believe that patients who are counseled appropriately will voluntarily inform relatives of the relevant information. In the small number of cases where patients object to such disclosures, they are unlikely to cooperate with disclosure attempts by health care providers, and identifying and tracking down the appropriate relatives may, as a practical matter, be impossible.

We recognize that there may be exceptional cases where a provider believes that disclosure of genetic information to a patient's relative is the only way to avert serious harm, but the patient is unwilling to consent to the information's release. In such circumstances, the law should allow the courts to determine the appropriateness of disclosure at a judicial hearing. Both the health care provider and the patient should be given an opportunity in that hearing to present evidence about whether the rare circumstances described above actually exist.

***Court Orders for Disclosure of Genetic Information***

**Other than court orders for the disclosure of genetic information to a patient's relatives, New York law should be amended to permit court orders for the disclosure of genetic information to third parties without the subject's consent only when (1) absent the disclosure, there is or would be a clear and imminent danger to the public health; (2) the third party is entitled to the disclosure under federal and/or New York statutes or regulations; or (3) in a civil or criminal litigation, the subject of the information affirmatively places his or her physical or mental condition at issue and the genetic information to be disclosed directly relates to that physical or mental condition.**

New York law currently permits courts to issue orders compelling disclosure of genetic information that is associated with future disease in oneself or one's offspring

after weighing "the privacy interests of the individual subject of the genetic test and of close relatives of such individual," as well as "the public interest."[232] We believe that this test is too malleable and permissive. It sets no criteria by which courts are to weigh the sometimes competing privacy interests of the subject, the privacy interests of the subject's close relatives, and the public interest. In addition, the test also can be interpreted as rendering the confidentiality protections for genetic information less rigorous than the protections afforded to other medical information. For example, courts may read the test as permitting disclosure of an individual's genetic information even if such a disclosure would have been forbidden under the physician-patient privilege.[233]

Other than court orders for the disclosure of genetic information to relatives, we believe that court-ordered disclosures of genetic information should be permitted only in the circumstances listed above.[234]

***Private Civil Remedies for Unlawful Disclosure or Solicitation of Genetic Information***

**Assuming that comprehensive medical confidentiality protections are not adopted, New York law should be amended to expressly authorize private lawsuits by victims of unlawful disclosures or solicitations of genetic information against persons who make such disclosures or solicitations. In cases where the unlawful disclosures or solicitations occur due to negligence, the victims should be authorized to recover actual damages for physical, emotional, and/or financial harms they suffer as a result. In cases where the unlawful disclosures or solicitations occur with knowledge that no consent has been obtained for such disclosures or solicitations, or where such unlawful disclosures or solicitations occur due to recklessness, victims should be authorized to recover actual damages for physical, emotional, and/or financial harms; punitive damages (in appropriate cases); and attorneys' fees. In cases where the unlawful disclosures or solicitations are performed willfully (i.e., with knowledge that the disclosures or solicitations are illegal), the victims should be authorized to recover statutory damages over and above any actual**

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[232] See page 261, this chapter.

[233] Cf. *Plaza v. Estate of Wisser*, 211 A.D.2d 111, 122–123, 626 N.Y.S.2d 446, 454 (N.Y. App. Div. 1995) (provision in HIV confidentiality law that permitted courts to order the disclosure of HIV-related information trumped the physician-patient privilege, which would have prohibited such a disclosure).

[234] An example of when a third party is entitled by statute to a disclosure of genetic information is the statutory right in New York of prospective adoptive parents to review the medical histories of prospective adoptees and their biological parents. See N.Y. Soc. Serv. Law § 373-a (McKinney 1999); Chapter 8, page 230.

**and punitive damages, even without proof of actual damages. New York law also should be amended to permit individuals to obtain injunctive relief to prevent unlawful disclosures or solicitations of and retention of unlawfully obtained genetic information.**

New York law currently authorizes patients to recover damages they actually suffer, as well as punitive damages, from *physicians* who disclose medical information, including genetic information, without consent. However, it is unclear whether the law authorizes private parties to recover for harms they suffer from other individuals (e.g., insurance companies) who solicit or disclose their genetic information in violation of the confidentiality provisions of New York's genetic confidentiality statutes. We can find no justification for conditioning the availability of damages on whether the source of the illegal disclosure or solicitation was a physician or someone else. In addition, the $1,000 and $5,000 fines currently authorized in the genetic testing statutes are too low to serve as effective deterrents, and, in any event, outside of the insurance context, they may be recovered by the state only if the violations are proven beyond a reasonable doubt.

Accordingly, we recommend that New York law be amended to expressly authorize individuals to recover damages from persons who unlawfully disclose or solicit genetic information and to obtain court orders to prevent further unlawful disclosures and solicitations. The different levels of damages we recommend are commensurate with the differing mental states and increasing culpability with which a person may disclose or solicit genetic information negligently, knowingly/recklessly, or intentionally. In addition, statutory damages should be set high enough to dissuade individuals from violating the informed consent requirements of the genetic testing statutes, and the standard of proof for recovery should be a preponderance of the evidence.

***Power of the Attorney General***

**Assuming that comprehensive medical confidentiality protections are not adopted, New York law should be amended to authorize the Attorney General to bring lawsuits on behalf of individuals whose genetic information has been unlawfully disclosed or solicited. New York law also should authorize the Attorney General to bring lawsuits to prevent such disclosures and solicitations. The Attorney General should be empowered to seek whatever relief individuals could seek if they brought the lawsuits themselves.**

Individuals may not have the resources to bring lawsuits to protect their rights under New York's genetic confidentiality statutes. Because society as a whole benefits from the vigorous enforcement of medical confidentiality protections, the Attorney General, as New York's chief legal officer, should have the authority to bring lawsuits on behalf of those unable or unwilling to sue themselves.

***Professional Discipline for Unlawful Disclosure or Solicitation of Genetic Information***

**Assuming that comprehensive medical confidentiality protections are not adopted, persons and organizations licensed by New York State should be subject to professional discipline for unlawfully disclosing or soliciting genetic information.**

Individuals and organizations who are licensed or certified by New York State, such as physicians, insurance companies, and health care organizations, are expected to follow the law. The possible suspension or loss of a license for unlawfully disclosing or soliciting genetic information can act as a powerful deterrent against such violations. Moreover, like actions by the Attorney General, disciplinary proceedings provide a mechanism for enforcing the genetic confidentiality laws that does not depend on the willingness of private parties to pay the costs associated with litigation.

***Internal Institutional Sanctions for Disclosure of Genetic Information***

**Private and public institutions that deal with genetic information should create their own internal sanctions against persons who unlawfully disclose or solicit genetic information.**

Internal institutional sanctions against individuals who unlawfully disclose or solicit genetic information are an additional deterrent and safeguard against such solicitations and disclosures. In addition, institutions that adopt such sanctions may lessen their exposure to liability for such actions.

***Anonymous Genetic Testing***

**Although anonymous genetic testing has significant drawbacks, it should be an option available to those who desire it. New York law should be amended to eliminate potential barriers to anonymous genetic testing.**

Anonymous genetic testing is of limited utility because determining what tests to perform and interpreting genetic test results properly generally require collecting a patient's family history information and, in some cases, may necessitate genetic testing of the patient's relatives. In addition, anonymous testing can interfere with proper patient follow-up and genetic counseling.

Nevertheless, we recognize that, no matter how clearly the law prohibits improper disclosures and solicitations of genetic information, such disclosures and solicitations

can occur and will be of particular concern to some individuals considering genetic testing. Anonymous genetic testing can serve as an additional safeguard against such occurrences. Because New York law concerning informed consent to genetic testing requires individuals to sign informed consent forms, the law can be interpreted to prohibit anonymous testing. New York law should be amended to make clear that such testing is permissible. That being said, health care providers should be free to exercise their professional judgment in deciding whether to perform anonymous genetic testing, and we anticipate that in many circumstances they will decide not to perform such testing.

# 10

## *The Use of Genetic Information in Insurance and Employment*

One of the public's greatest concerns about genetic testing is that test results will be used against individuals to deny them insurance or employment.[1] This fear is so pervasive that a 1996 study by the National Center for Genome Resources found that 63 percent of the public would probably not or definitely not take genetic tests if insurers or employers had access to them.[2]

The public's fear has some basis in historical fact. In the 1970s, large-scale sickle cell disease testing programs were implemented.[3] Based on one scientific paper that was later refuted, over 25 percent of the life insurance companies in the United States charged higher premiums for people who were carriers of the sickle cell gene mutation even though they did not have, and would never develop, sickle cell disease. In addition, sickle cell mutation gene carriers were excluded from certain industrial positions deemed "high risk," from being commercial airline pilots, and from pilot training in the United States Air Force Academy.[4]

### The Use of Genetic Information in Insurance

Currently, insurers do not require applicants to take predictive genetic tests because the tests are very expensive and reveal only a limited number of serious genetic abnormalities.[5] However, insurers have argued that they are entitled to learn the results of

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[1] See American Medical Association, AMA Survey: Americans Trust Physicians on Genetic Testing Information (Press Release, March 11, 1998).

[2] National Center for Genome Resources, "National Survey of Public Stakeholders Attitudes and Awareness of Genetic Issues," National Center for Genome Resources website: *http://www.ncgr.org/gpi/survey/results/exec_sum.html*, visited March 12, 1998.

[3] For a discussion of these programs, see Chapter 5, page 114.

[4] R. Murray, "The Ethics of Predictive Genetic Screening: Are the Benefits Worth the Risks?" in *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp (Tuskegee, AL: Tuskegee University, 1997), 139, 145–146.

[5] See American Academy of Actuaries, "Genetic Information and Voluntary Life Insurance," American Academy of Actuaries website: *ftp://www.actuary.org/pub/actuary.org/issuebrf/genet.pdf*, visited February 22, 1999; C. S. Jones, "The Rush to Legislate: An Insurance Industry Perspective on the Current State of Genetic Testing," *Contingencies* (November/December 1998): 18, 23; R. M. Berry, "The Human Genome Project and the End of Insurance," *University of Florida Journal of Law and Public Policy* 7 (1996): 205, 235; N. E. Kass "The Implications of Genetic Testing for Health and Life Insurance," in *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*, ed. M. A. Rothstein (New Haven, CT: Yale University Press, 1997), 299, 303; American Academy of Actuaries, "Genetic Information and Voluntary Life Insurance," American Academy of Actuaries website: *ftp://www.actuary.org/pub/actuary.org/issuebrf/genet.pdf*, visited May 15, 2000.

genetic tests that insurance applicants have taken in other contexts.[6] As genetic tests become more informative and affordable, health and life insurers may require applicants to take such tests and to reveal the results of genetic tests that they have previously taken.[7]

Even without performing genetic tests, insurance companies may learn genetic information about individuals through questions about their family and medical histories, examination of their medical records, and the performance of nongenetic medical testing.[8] A 1992 survey of health insurers by the Office of Technology Assessment revealed that family medical history was one of the two most important factors that health insurers use to determine insurability.[9] However, a recent study found that health insurers use family history "only occasionally and only to find out more information about existing conditions."[10]

A number of studies have concluded that insurers use genetic information to make adverse insurance decisions.[11] By contrast, other studies have found that, at least in the health insurance context, insurance companies are generally not using genetic information in making coverage decisions.[12] In addition, a number of commentators claim that the

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[6] Michigan Commission on Genetic Privacy and Progress, *Final Report and Recommendations* (Lansing, MI: Michigan Commission on Genetic Privacy and Progress, 1999), 24; Kass, "The Implications of Genetic Testing for Health and Life Insurance," 303–304.

[7] Kass, "The Implications of Genetic Testing for Health and Life Insurance," 303–304; M. A. Hall and S. S. Rich, "Laws Restricting Health Insurers' Use of Genetic Information: Impact on Genetic Discrimination," *American Journal of Human Genetics* 66 (2000): 293, 303; American Academy of Actuaries, "Genetic Information and Voluntary Life Insurance," American Academy of Actuaries website: *ftp://www.actuary.org/pub/actuary.org/issuebrf/genet.pdf*, visited May 15, 2000.

[8] J. Beckwith and J. S. Alper, "Reconsidering Genetic Antidiscrimination Legislation," *Journal of Law, Medicine and Ethics* 26 (1998): 205, 206; G. Held, "Testing the Waters in the Gene Pool," *Contingencies* (November/December 1998): 25, 27; Berry, "The Human Genome Project and the End of Insurance," 235.

[9] Office of Technology Assessment, *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening* (Washington, D.C.: U.S. Government Printing Office, 1992).

[10] Hall and Rich, "Laws Restricting Health Insurers' Use of Genetic Information," 303. See also American Academy of Actuaries, "Risk Classification in Individually Purchased Voluntary Medical Expense Insurance," American Association of Actuaries website: *http://www.actuary.org/pub/actuary.org/issuebrf/risk.pdf*, visited April 21, 1999. The study did find "a few cases of discrimination based on family history." Hall and Rich, "Laws Restricting Health Insurers' Use of Genetic Information," 303.

[11] See, e.g., E. V. Lapham, C. Kozma, and J. O. Weiss, "Genetic Discrimination: Perspectives of Consumers," *Science* 274 (1996): 274; P. R. Billings et al., "Discrimination as a Consequence of Genetic Testing," *American Journal of Human Genetics* 50 (1992): 476.

[12] Hall and Rich, "Laws Restricting Health Insurers' Use of Genetic Information," 302; S. M. Kopinsky, "Genetic Discrimination Is Less Widespread Than Feared," Health Care News Server website: *http://www.healthcarenewsserver.com*, visited June 30, 1999.

anecdotal evidence used by many of the studies that found adverse use of genetic information by insurance companies overestimated the frequency of such decisions.[13]

Some commentators argue that if insurers are permitted to use genetic information, individuals who could potentially benefit from genetic testing may refrain from undergoing it and may thereby endanger their health.[14] Physicians at Memorial Sloan Kettering Cancer Center report that 60 percent of patients who undergo genetic counseling for BRCA1 testing decline to take that test; the most common reason cited for that decision is fear of insurance and employment discrimination.[15] In addition, commentators argue that concerns about the use of test results in insurance and employment may inhibit individuals' willingness to participate in genetic research.[16] For example, about 33 percent of people asked to participate in a study on maintaining the health of persons with genetic predispositions to cancer refused to participate out of fear of discrimination and loss of privacy.[17] Citing similar concerns, 32 percent of people asked refused to take genetic tests that were part of National Institutes of Health genetic research studies on breast cancer.[18]

Other commentators claim that the use of genetic information by insurers is akin to racial and ethnic discrimination because genetic traits are predetermined and are beyond an individual's control.[19] These commentators maintain that to permit insurers to use this information would be inconsistent with "cherished beliefs in justice and equality."[20]

By contrast, insurers argue that the "cornerstone" of the private insurance industry is the ability to engage in what they term "fair discrimination," that is, the ability to make decisions about premiums and coverage commensurate with each individual's risk.[21] Insurers contend that "the goal is not equal treatment of policyholders, but equitable

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[13] See, e.g., A. Buchanan, "Ethical Responsibilities of Patients and Clinical Geneticists," *Journal of Health Care Law and Policy* 1 (1998): 391, 398; M. K. Mansoura and F. S. Collins, "Medical Implications of the Genetic Revolution," *Journal of Health Care Law and Policy* 1 (1998): 329, 344.

[14] See Mansoura and Collins, "Medical Implications of the Genetic Revolution," 344; Statement of F. S. Collins, "Health Insurance in the Age of Genetics," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/NEWS/insurance*, visited January 26, 1999.

[15] See G. B. Mann and P. I. Brogan, "Breast Cancer Genes and the Surgeon," *Journal of Surgical Oncology* 67 (1998): 267, 272.

[16] See Mansoura and Collins, "Medical Implications of the Genetic Revolution," 344; Statement of F. S. Collins, "Health Insurance in the Age of Genetics," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/NEWS/insurance*.

[17] Statement of F. S. Collins, "Health Insurance in the Age of Genetics," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/NEWS/insurance*.

[18] Ibid.

[19] Council for Responsible Genetics, "Position Paper on Genetic Discrimination," Council for Responsible Genetics website: *http://www.gene-watch.org/gendisc.html*, visited June 1, 1999; J. Gaulding, "Race, Sex, and Genetic Discrimination in Insurance: What's Fair?" *Cornell Law Review* 80 (1995): 1646, 1648–1649.

[20] Council for Responsible Genetics, "Position Paper on Genetic Discrimination," Council for Responsible Genetics website: *http:www.gene-watch.org/gendisc.html*, visited June 1, 1999.

[21] See Panel Discussion, "Government and Public Policy in the United States: What Should Be the Role of State and Federal Government in Regulating Genetic Data?" *Suffolk University Law Review* 27 (1993): 1547, 1548; R. B. Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite on the Basis of Genetic Information and Genetic Test Results," *Suffolk University Law Review* 27 (1993): 1271, 1286–1287.

treatment," and that it is inequitable to charge persons with different levels of risk the same amount for the same insurance products.[22] To prohibit the use of genetic information in underwriting, insurers contend, will force them to charge higher rates for "healthy insureds" to pay for the cost of underwriting individuals who have genetic conditions or identifiable predispositions about which the insurers will be forbidden to ask or take into account.[23] Moreover, such a prohibition will unfairly give preferential treatment to individuals who have genetic conditions or identifiable predispositions because insurers will be forced to sell them insurance at standard rates while other insureds, who have an equal risk of illness or death from unidentified genetic predispositions or nongenetic causes, can be charged higher premiums or denied insurance.[24]

Insurers also argue that prohibiting the use of genetic information for insurance underwriting will lead to adverse selection. That is, individuals who are aware that they have genetic predispositions to disease will buy more insurance, and insurers, who will be denied knowledge about applicants' genetic predispositions, will have to raise insurance rates for all insureds to pay for the increased risks. The higher insurance costs will cause persons who perceive themselves as having lower health risks to stop purchasing insurance, leaving the insurance pool with a larger percentage of people with a higher-than-average risk of loss. That, in turn, will cause insurers to raise their rates even further, again causing more lower-risk people to leave the insurance pool.[25] According to insurers, this cycle, know as an "assessment spiral," will continue until "either an equilibrium is reached with some of the low-risk insureds still buying insurance" or the premiums become so high that no one purchases insurance.[26] Insurers also maintain that if they are prohibited from using genetic

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[22] Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite on the Basis of Genetic Information and Genetic Test Results," 1287 (internal quotation marks omitted).

[23] See ibid., 1288; E. M. Holmes, "Solving the Insurance/Genetic Fair/Unfair Discrimination Dilemma in Light of the Human Genome Project," *Kentucky Law Journal* 85 (1997): 503, 534, 537–541; Kass, "The Implications of Genetic Testing for Health and Life Insurance," 301; National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Information and Insurance, *Genetic Information and Health Insurance* (Washington, D.C.: National Institutes of Health, 1993), 16; D. A. Stone, "The Implications of the Human Genome Project for Access to Health Insurance," in *The Human Genome Project and the Future of Health Care*, ed. T. H. Murray, M. A. Rothstein, and R. F. Murray, Jr. (Bloomington: Indiana University, 1996), 133, 135–137.

[24] Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite on the Basis of Genetic Information and Genetic Test Results," 1287 & n.90. See M. A. Rothstein, "Genetic Privacy and Confidentiality: Why They Are So Hard to Protect," *Journal of Law, Medicine and Ethics* 26 (1998): 198, 199–200.

[25] J. Herman, "Genetic Testing and Insurance: A Question of Balance," in *Plain Talk about the Human Genome Project*, ed. E. Smith and W. Sapp (Tuskegee, AL: Tuskegee University, 1997), 179, 179–181; Holmes, "Solving the Insurance/Genetic Fair/Unfair Discrimination Dilemma," 544; NIH-DOE Task Force on Genetic Information and Insurance, *Genetic Information and Health Insurance*, 16.

[26] Holmes, "Solving the Insurance/Genetic Fair/Unfair Discrimination Dilemma," 544; NIH-DOE Task Force on Genetic Information and Insurance, *Genetic Information and Health Insurance*, 16.

information for medical underwriting, they could be rendered insolvent or incapable of paying plan benefits.[27]

Finally, insurers point out that, in the current medical underwriting system, the question of whether individuals have control over their health conditions is irrelevant; insurers are concerned only about the probability of illness and death.[28] Arguing that there is no clear understanding of what risk factors are within an individual's control, they maintain that an insurance system based on the insureds' "fault" would be arbitrary and unfair.[29]

In response to insurers' adverse selection arguments, some commentators assert that there is little empirical evidence that adverse selection actually takes place in insurance markets.[30] At least in the individual and small group health insurance market, there is some evidence that adverse selection does not generally occur.[31] That may be because consumers are "uninformed about their true risk of loss," are "bad at probabilistic thinking," or "may be sufficiently risk averse to purchase insurance above its actuarial value."[32] There is also some preliminary evidence that indicates that women who test positive for a BRCA1 mutation do not purchase more life insurance than women who have not undergone genetic testing for the mutation and have first- or second-degree relatives who have had breast or ovarian cancer.[33]

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[27] See, e.g., Herman, "Genetic Testing and Insurance," 181; Holmes, "Solving the Insurance/Genetic Fair/Unfair Discrimination Dilemma in Light of the Human Genome Project," 543–545; D. A. Stone, "The Implications of the Human Genome Project for Access to Health Insurance," in *The Human Genome Project and the Future of Health Care* (Bloomington: Indiana University, 1996), 133, 135–137.

[28] See Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite on the Basis of Genetic Information and Genetic Test Results," 1297–1298.

[29] Ibid.

[30] See, J. V. Jacobi, "The Ends of Health Insurance," *University of California at Davis Law Review* 30 (1997): 311, 387–393; Panel Discussion, "Government and Public Policy in the United States," 1547, 1552 (comment of Dr. Paul Billings); Stone, "The Implications of the Human Genome Project for Access to Health Insurance,"136. Even a commentator from the insurance industry concedes that, at least in the life insurance context, there is no virtually no evidence of adverse selection occurring, although she attributes that to the fact that "life insurers have not thus far been deprived of the means with which to control [adverse selection]." See Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite on the Basis of Genetic Information and Genetic Test Results," 1290.

[31] Jacobi, "The Ends of Health Insurance," 390–391; F. A. Sloan and C. J. Conover, "Effects of State Reforms on Health Insurance Coverage of Adults," *Inquiry* 35 (1998): 280 ("Recent studies have not found that community rating results in a general exodus of health plans or in large scale disenrollment."); L. M. Nichols, "State Regulation: What Have We Learned So Far?" *Journal of Health Politics, Policy and Law* 25 (2000): 175, 194. But see Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite on the Basis of Genetic Information and Genetic Test Results," 1290 (claiming in 1993 that there may be some evidence that New York's community rating laws are leading to adverse selection).

[32] Jacobi, "The Ends of Health Insurance," 389, 392–393. Consumers routinely pay insurance premiums that are higher than the actuarially accurate cost of the insurance. Ibid., 389.

[33] See C. D. Smith et al., "Genetic Testing, Adverse Selection, and the Demand for Life Insurance," *American Journal of Medical Genetics* 93 (2000): 29.

## Health Insurance

According to the 1997 United States Census, 83.9 percent of Americans are covered by some form of health insurance. Employers provide health insurance for 61.4 percent of the population, 8.7 percent of the population purchases their health insurance from other private sources, and 24.8 percent of the population has some form of government health insurance such as Medicare or Medicaid.[34]

### *Individual Health Insurance*

Approximately 10 to 15 percent of the private health insurance sold in the United States is individual health insurance,[35] that is, health insurance that individuals purchase individually for themselves and their families.[36] Subject to restrictions contained in state and federal law, coverage and premium decisions for individual health insurance policies may be based on individuals' health status and medical histories.[37] For example, some health insurers deny coverage altogether to people with AIDS or diabetes, charge higher premiums for people with hypertension or anemia, and/or offer general health coverage while excluding from coverage pre-existing conditions, that is, conditions that individuals had before applying for coverage.[38] When insurance companies make coverage and premium decisions based on an individual's health condition and medical history, they are engaging in a process known as medical underwriting.[39]

Many states have enacted laws that limit health insurers' freedom to medically underwrite in the individual health insurance market.[40] For example, some states require health insurers to offer at least one health insurance plan in which all applicants must be accepted regardless of their health status or medical history.[41] Other states require insurers to renew health insurance policies regardless of the insureds' health status or previous claims under the policy.[42] Still other states restrict the premiums that health insurance companies may charge for individual health insurance policies.[43] Nevertheless, a number of states have

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[34] United States Census Bureau, *Health Insurance Coverage: 1997*, United States Census Bureau website: *http://www.census.gov/prod/3/98pubs/p60-202.pdf*, visited February 23, 1999. These statistics reflect that some people are covered by more than one type of health insurance. Ibid.

[35] See N. E. Kass, "The Implications of Genetic Testing for Health and Life Insurance," 300.

[36] United States General Accounting Office, *Private Health Insurance: Millions Relying on Individual Market Face Cost and Coverage Trade-Offs* (Washington, D.C.: U.S. General Accounting Office, 1996), 2.

[37] Ibid., 42; K. H. Rothenberg, "Genetic Information and Health Insurance: State Legislative Approaches," *Journal of Law, Medicine and Ethics* 23 (1995): 312, 312.

[38] U.S. General Accounting Office, *Private Health Insurance*, 43; Jacobi, "The Ends of Health Insurance," 369–376.

[39] U.S. General Accounting Office, *Private Health Insurance*, 42.

[40] Ibid., 52–61.

[41] Ibid., 56.

[42] Ibid., 57.

[43] Ibid., 58.

few, if any, restrictions on insurance rates and fail to provide other insurance mechanisms for persons insurers will not fully insure.[44]

Under the federal Health Insurance Portability and Accountability Act (HIPAA) individual insurers are required to issue health insurance policies to individuals who had coverage for the previous eighteen months under a "group health plan, governmental plan or church plan."[45] HIPAA places no limit on the premiums the insurer may charge for these policies.[46]

New York law regulates the individual and small group (up to fifty persons) health insurance markets through a system of community rating and open enrollment. Under New York's community rating law, New York State is divided into geographic areas. The law mandates that within a given geographic area, health insurance premiums must be identical for all individual health policies, regardless of health, age, sex, or occupation, and must be "based on the experience of the entire pool of risks" covered by the policy.[47] New York law specifically prohibits insurers who issue individual and small group insurance policies from obtaining information about individuals' medical histories and from requiring medical and laboratory tests or medical examinations of insurance applicants.[48] Under open enrollment, all individuals and small groups that apply for health insurance must be accepted any time they apply and may not be terminated from coverage or refused policy renewal because of their claims history.[49]

Under some circumstances, however, New York law permits health insurers who issue individual health insurance policies to exclude from coverage pre-existing conditions for up to twelve months after an individual enrolls.[50] The pre-existing condition exclusion applies to conditions "for which medical advice, diagnosis, care or treatment was recommended or received" during the six months prior to enrolling in the plan.[51] That twelve-month period is reduced by the number of months the individual was covered by health insurance prior to enrolling in the new plan.[52]

Thus, for example, if three months before obtaining health insurance, a previously uninsured individual was diagnosed with asthma, the insurer could refuse to cover the costs of the individual's asthma care for up to the first twelve months of the policy. If the individual had health insurance for the previous eight months, the insurer could refuse to cover the costs of the asthma care for the first four months of the policy.

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[44] Ibid., 52.

[45] 42 U.S.C.A. 300gg-41(b) (West 1999); R. E. Rosenblatt, S. A. Law, and S. Rosenbaum, *Law and the American Health Care System* (New York: The Foundation Press, Inc., 1997), 319–320.

[46] Rosenblatt, Law, and Rosenbaum, *Law and the American Health Care System*, 322.

[47] 11 N.Y.C.R.R. § 360.2(b) (1998); N.Y. Ins. Law § 3231(a) (McKinney 1999); *Colonial Life Ins. Co. of America v. Curiale*, 205 A.D.2d 58, 60 n.1, 617 N.Y.S.2d 377, 379 n.1 (N.Y. App. Div. 1994); Meeting with Insurance Advisory Committee, Albany, New York, February 17, 1999.

[48] See N.Y. Ins. Law §§ 4317(a), 3231(a) (McKinney 1999); 11 N.Y.C.R.R. § 360.5a (2), (3), (5), (6), (7) (1999).

[49] See N.Y. Ins. Law §§ 4317(a), 3231(a) (McKinney 1999).

[50] Ibid., §§ 3231, 3232(b), 4317(a), 4318(b).

[51] Ibid., §§ 3232(b), 4318(b).

[52] Ibid., §§ 3232 (a), (c), 4318(a), (c).

New York law specifically prohibits individual and small group health insurers from using genetic information as a pre-existing condition in the absence of a diagnosis of a condition related to the information.[53]

Since the early 1990s, a growing number of states have passed legislation that limits the ability of insurers to utilize genetic information in medical underwriting of health insurance.[54] Some of these laws prohibit health insurers from using genetic information or genetic test results to establish eligibility, set premiums, or limit coverage for health insurance.[55] A number of these laws also prohibit health insurers from requesting or requiring the provision of genetic information as a condition of obtaining insurance.[56] Nevertheless, at least two state laws that generally do not permit health insurers to utilize or request genetic information permit health insurers to utilize such information if individuals voluntarily submit it to the companies and the information is favorable to the individuals.[57]

As a result of community rating and open enrollment, New York health insurers who issue individual health insurance policies cannot utilize or ask about genetic information for medical underwriting purposes. In addition, New York law prohibits insurers from placing an individual's genetic test results into a nonconsenting relative's records, and also prohibits the insurers from drawing, using, or communicating an adverse inference about the relative's genetic status based on these results.[58] The law also prohibits insurers from disclosing an individual's genetic test results to third parties unless authorized to do so by the insured.[59]

Commentators disagree about the wisdom of laws that specifically limit the ability of insurers to take into account genetic information in coverage and underwriting decisions. While many commentators, including the American Medical Association, endorse such laws,[60] others argue that attempting to distinguish between "genetic" and "nongenetic"

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[53] Ibid., §§ 3232 (b), 4318(b).

[54] Rothenberg, "State Legislative Approaches," 313; American Society of Human Genetics, February 1999 Newsletter, American Society of Human Genetics website: *http://www.faseb.org/genetics/ashg/newsletr/news-02.htm*, visited March 22, 1999.

[55] See., e.g., Haw. Rev. Stat. Ann. § 431:10A-118 (a)(1) (Michie 1999); Fla. Stat. Ann. § 627.4301(2)(a) (West 1999); Ind. Code Ann. § 27-8-26-8 (West 2000).

[56] See, e.g., Haw. Rev. Stat. Ann. § 431:10A-118(a)(2) (Michie 1998); Fla. Stat. Ann. § 627.4301(2)(b) (West 1999); Ind. Code Ann. § 27-8-26-6 (West 2000).

[57] See Ind. Code Ann. § 27-8-26-9 (West 2000); 410 Ill. Comp. Stat. Ann. § 513/20(b) (West 1999).

[58] See N.Y. Ins. Law § 2612(h) (McKinney 1999). Insurers also may not use genetic test results they had in their possession prior to November 6, 1996, the effective date of New York's genetic testing statutes, to take adverse actions against the subjects of those tests. Ibid., § 2612(f).

[59] Ibid., § 2612(f).

[60] See, e.g., American Medical Association, House of Delegates Resolution H-185.972 (1998); American Medical Association, "Genetic Information and Insurance Coverage," Board of Trustees Report 15 (I-96) of the American Medical Association, December 1996; K. L. Hudson et al., "Genetic Discrimination and Health Insurance: An Urgent Need for Reform," *Science* 270 (1995): 391. The American Medical Association also contends that physicians should not participate in predispositional genetic testing by

factors is unworkable. In 1993, the National Institutes of Health-U.S. Department of Energy Working Group on Ethical Legal, and Social Implications of Human Genome Research Task Force on Insurance (NIH-DOE Task Force on Insurance) argued that a large amount of information about health risks, such as cholesterol level, and many common diseases, such as cancer and heart disease, cannot be classified as wholly genetic or nongenetic but result from "a complex set of interactions of both genetic and nongenetic factors."[61] Therefore, the NIH-DOE Task Force on Insurance opposed specific prohibitions against the use of genetic information in insurance decisions.[62] Rather, it maintained that health care is a social good

that should be accessible to all and recommended the adoption of universal health care and the elimination of risk-based health insurance.[63] A 1994 Institute of Medicine Committee on Assessing Genetic Risks (IOM Committee) concurred with these conclusions and recommendations.[64]

### *Group Health Insurance*

Group health insurance, which accounts for 85 to 90 percent of the private health insurance sold in the United States, is health insurance that is purchased by a group of people rather than by an individual.[65] A typical example of group insurance is insurance that employers provide as a benefit to their employees.[66] Insurance premiums for groups are usually not based on individual health assessments of the group's members. Rather, in a process known as "experience rating," insurers set premiums based on the group's past health insurance claims as well as the group's age and gender composition.[67] Nevertheless, some insurers have used individual underwriting in the past to aid in setting health insurance premiums for groups, while others use individual underwriting only to set premiums for small groups.[68]

New York and federal law prohibits group health plans from charging higher premiums or refusing to provide coverage for an individual based on the individual's health status, medical history, or genetic information.[69] Federal law permits group health plans to charge higher premiums to an entire group if an individual member of the group is at higher

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insurance companies. American Medical Association, Council of Ethical and Judicial Affairs, E-2.135 (1998).

[61] NIH-DOE Task Force on Genetic Information and Insurance, *Genetic Information and Health Insurance*, 8.

[62] Ibid., 8–10.

[63] See ibid., 9–11.

[64] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 281.

[65] See Kass, "The Implications of Genetic Testing for Health and Life Insurance," 300.

[66] Ibid.

[67] Ibid.; Meeting with Insurance Advisory Committee, Albany, New York, February 17, 1999.

[68] Stone, "The Implications of the Human Genome Project," 144–145. See generally D. A. Engel, "The ADA and Life, Health, and Disability Insurance: Where Is the Liability?" *Tort and Insurance Law Journal* 33 (1997): 227 (noting that group health insurers have engaged in individual medical underwriting).

[69] See 29 U.S.C.A. § 1182 (West 2000); N.Y. Ins. Law § 3221(q) (McKinney 1999).

risk,[70] and New York law does not prohibit this practice for group health plans over fifty persons. Thus, for example, a group health insurer may not charge a higher insurance premium to an individual who has a genetic predisposition to breast cancer, but the insurer can raise the rates for the entire group to pay for the extra risk. Both HIPAA and New York law prohibits group health insurers from treating genetic information as a pre-existing condition "in the absence of a diagnosis of the condition related to such information."[71]

### Life, Disability, and Long-Term Care Insurance

#### *New York Insurance Law*

New York insurance law generally permits life, disability, and long-term care insurers to individually underwrite insurance using whatever factors they choose, as long as there is a proper underwriting basis for doing so.[72] Although individuals can file complaints against insurers with the New York State Insurance Department challenging the actuarial or other underwriting basis of insurers' underwriting practices, and the Insurance Department has the power and duty to adjudicate such complaints,[73] few, if any, individuals have actually done so.[74] If such a complaint were filed, the Insurance Department might give considerable deference to the actuarial calculations and underwriting justifications of the insurance companies.[75]

Under certain circumstances, New York's insurance law permits insurers to provide different terms and conditions of insurance based on an individual's disability,[76]

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[70] See 29 U.S.C.A. § 1182 (b)(2)(A) (West 2000).

[71] 29 U.S.C.A. § 1181(b)(1)(B) (West 2000); N.Y. Ins. Law §§ 3232 (b), 4318(b) (McKinney 1999).

[72] See *Matter of Health Ins. Ass'n of America v. Corcoran*, 154 A.D.2d 61, 67–69, 551 N.Y.S.2d 615, 618–19 (N.Y. App. Div.) (internal quotation marks omitted), *aff'd on opinion below*, 76 N.Y.2d 995, 564 N.Y.S.2d 713 (1990); N.Y. Ins. Law §§ 4224(a)(1), (a)(2), (b)(1), (b)(2), 1113(a)(3), 1117(a) (McKinney 1999).

[73] "The Insurance Department has the statutory power and duty to determine whether policy premiums are rationally related to risks and expenses and to eliminate discriminatory practices in the writing of insurance." *Binghamton GHS Employees Federal Credit Union v. State Division of Human* Rights, 77 N.Y.2d 12, 16–17, 563 N.Y.S.2d 385, 387 (1990) (internal citations omitted). See N.Y. Ins. Law §§ 2606, 2607, 3201(c); 4224 (McKinney 1999).

[74] Meeting with Insurance Advisory Committee, Albany, New York, February 17, 1999. Some individuals have brought lawsuits against insurers claiming that the insurers' practices were not actuarially justified and did not have a proper underwriting basis. See *Dornberger v. Metropolitan Life Ins. Co.*, 961 F. Supp. 506, 547–548 (S.D.N.Y. 1997) (refusing motion to dismiss claim under Section 4224 against an insurance company). Cf. *Pallozzi*, 198 F.3d 28, 30, 36 n.6 (2d Cir. 1999) (permitting lawsuit under the Americans with Disabilities Act to go forward on the theory that the defendants violated section 4224), *amended on denial of reh'g*, 204 F.3d 392 (2d Cir. 2000).

[75] Meeting with Insurance Advisory Committee, Albany, New York, February 17, 1999. See Rothstein, "Genetic Privacy and Confidentiality," 200 (state regulators traditionally show great deference to the actuarial calculations of insurance companies).

[76] N.Y. Ins. Law § 2606 (a), (d).

gender,[77] or marital status.[78] However, insurers may not differentiate in the terms and conditions of insurance based on race, color, creed, or national origin.[79]

At least one state has enacted a law that prohibits group disability and/or long-term care insurers from underwriting based on genetic information, and another state has prohibited insurers from requiring individuals to undergo genetic testing in order to qualify for life, disability, and/or long-term care insurance.[80] New York has not enacted such prohibitions. Some states allow the use of genetic information for medical underwriting for life, disability, and/or long-term care insurance but require an actuarial or claims experience basis for such underwriting.[81]

New York's insurance law provides that before insurers may have genetic tests performed on individuals, the insurers must obtain the individuals' written informed consent.[82] In addition, if an insurer charges an individual a higher-than-standard premium or denies the individual insurance based on genetic test results, it must notify the individual in writing.[83] New York law prohibits insurers from placing an individual's genetic test results into a nonconsenting relative's records and also prohibits insurers from drawing, using, or communicating an adverse inference about the relative's genetic status based on these results.[84]

### *Life Insurance*

The majority of life insurance sold in the United States consists of individual policies that are individually underwritten.[85] The remainder consists of group life insurance policies that are largely not individually underwritten.[86] However, under certain circumstances, such as life insurance for small groups, late entrants into a group, and individuals who purchase large supplemental life insurance policies in addition to their group life insurance coverage, individuals who purchase life insurance may be

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[77] See *National Org. for Women v. Metropolitan Life Ins. Co.*, 131 A.D.2d 356, 358–359, 516 N.Y.S.2d 934, 936–937 (N.Y. App. Div. 1987). However, insurers are prohibited from denying insurance to an individual based on gender. See N.Y. Ins. Law § 2607 (McKinney 1999).

[78] Ibid. Although insurers are permitted to deny insurance based on disability under certain circumstances, ibid., § 2606(e), they are prohibited from doing so based on marital status. N.Y. Ins. Law § 2607 (McKinney 1999).

[79] See *National Org. for Women v. Metropolitan Life Ins. Co.*, 131 A.D.2d at 358, 516 N.Y.S.2d at 935; N.Y. Ins. Law § 2606(a), (b) (McKinney 1999).

[80] See Colo. Rev. Stat. Ann. § 10-3-1104.7 (1)(d), (3)(b) (West 1999); Vermont Stat. Ann. Tit. 10 § 9334 (West 1999).

[81] See, e.g., New Mexico Stat. Ann. § 24-21-4 (c)(1999); Maine Rev. Stat. Ann. Tit. 24-A § 2159-C(3) (West 1999).

[82] N.Y. Ins. Law § 2612(a) (McKinney 1999).

[83] See N.Y. Ins. Law § 2612(e), (i); 2611(d)(1) (McKinney 1999). For the definition of genetic test under New York law, see Chapter 9, page 260.

[84] See N.Y. Ins. Law § 2612(h) (McKinney 1999). Insurers also may not use genetic test results they had in their possession prior to November 6, 1996, the effective date of New York's genetic testing statutes, to take adverse underwriting actions against the subjects of those tests. Ibid., § 2612(f).

[85] Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite," 1280.

[86] Ibid.

subject to individual underwriting.[87] Approximately 62 percent of New Yorkers with life insurance have individual coverage, and 38 percent have group coverage.[88] Approximately 85 to 90 percent of New Yorkers who have group life insurance coverage obtain it through their employers.[89]

Life insurance has multiple social purposes.[90] While all life insurance provides money to an insured's beneficiaries after the insured dies, some types of policies are also investment vehicles that can pay dividends to the insured while the insured is alive.[91]

Contending that, except for certain single-gene disorders,[92] there are currently insufficient actuarial data to justify the use of genetic information as an accurate predictor of mortality, a number commentators have argued that a moratorium should be placed on the use of genetic information by life insurers.[93] Others claim that genetic information associated with certain multifactorial genetic diseases[94] can provide useful information for insurers.[95]

Some commentators contend that society has not traditionally viewed life insurance as a basic right and that life insurers should be permitted, at least to some extent, to use genetic information in underwriting decisions.[96] The American Medical Association (AMA) has expressed reservations about prohibiting life insurers from underwriting based on genetic information because of concerns about adverse selection and because the AMA contends that

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[87] Ibid.

[88] Meeting with Insurance Advisory Committee, Albany, New York, February 17, 1999.

[89] Ibid.

[90] Dr. Thomas Murray, President, The Hastings Center, Garrison, New York, presentation to the New York State Task Force on Life and the Law, February 24, 1999.

[91] See D. R. Fischel and R. S. Stillman, "The Law and Economics of Vanishing Premium Life Insurance," *Delaware Journal of Corporate Law* 22 (1997): 1, 3–6 (discussing various types of "whole life" life insurance).

[92] A single-gene disorder is a genetic disorder in which inheritance of a mutant gene or pair of mutant genes correlates 100 percent with disease incidence.

[93] Human Genetics Advisory Commission, "The Implications of Genetic Testing for Insurance," Human Genetics Advisory Commission website: *http://www.dti.gov.uk/hgac*, visited June 2, 1999; T. Wilkie, "Genetics and Insurance in Britain: Why More Than Just the Atlantic Divides the English Speaking Nations," *Nature Genetics* 20 (1998): 119, 120. See also Rothstein, "Genetic Privacy and Confidentiality," 200.

[94] For a definition of multifactorial genetic disease, see Chapter 1, page 17.

[95] Wilkie, "Genetics and Insurance in Britain," 120.

[96] Meyer, "Justification for Permitting Life Insurers to Continue to Underwrite on the Basis of Genetic Information and Genetic Test Results," 1292–1293. See also R. A. Bornstein, "Genetic Discrimination, Insurability and Legislation: A Closing of Legal Loopholes," *Journal of Law and Policy* (1996): 551, 608; T. H. Murray, "Genetics and the Moral Mission of Health Insurance," *Hastings Center Report* 22 (1992): 12, 15–16.

the "need for life insurance is not as compelling as that for health insurance."[97] The IOM Committee maintains that life insurance is unlike health insurance because it does not regulate access to "an important social good" such as health care.[98] However, the IOM Committee and other commentators recommend that individuals should be entitled to a limited amount of life insurance without regard to health or genetic status.[99] Some commentators have noted that life insurers currently sell policies that do not require any underwriting, although the insurers may charge higher rates for these policies and they may only be for small amounts.[100]

***Disability Insurance***

Disability insurance reimburses individuals for income they lose if they become unable to perform their occupations due to physical or mental disability.[101] Disability insurance policies typically pay insureds 60 to 70 percent of their salaries; they generally pay less than the insured's full salary in order to give the insured an economic incentive to return to work.[102] Short-term disability insurance generally provides coverage for three to six months, while long-term disability insurance provides coverage for disabilities that last longer.[103] The federal government provides limited disability benefits through the Social Security program.[104]

Like life insurance, disability insurance can be seen as a means to protect assets, as opposed to a means of accessing "an important social good" such as health care.[105] One commentator has argued that, in our society, disability insurance is generally not regarded as a right but as "an optional commercial transaction." As a result, this commentator contends, all relevant information, including genetic information, should be available to both parties.[106]

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[97] "Genetic Information and Insurance Coverage," Board of Trustees Report 15 (I-96) of the American Medical Association, December 1996, at 86.

[98] See Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 281.

[99] See ibid., 280; M. A. Rothstein, "Genetic Secrets: A Policy Framework," in *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era*, ed. M. A. Rothstein (New Haven, CT: Yale University Press, 1997), 451, 474.

[100] Panel Discussion, "Government and Public Policy," 1552 (comment of Dr. Paul Billings); Meeting with Insurance Advisory Committee, Albany, New York, February 17, 1999; Rothstein, "Genetic Secrets: A Policy Framework," 474.

[101] See K. S. Abraham and L. Liebman, "Private Insurance, Social Insurance, and Tort Reform: Toward a New Vision of Compensation for Illness and Injury," *Columbia Law Review* 93 (1993): 75, 81.

[102] Insuremarket, "Disability Income Insurance Basics," website: *http://www.insuremarket.com/basics/disability/disbasics.htm*, visited June 2, 1999.

[103] Bureau of Labor Statistics, 1992 Employee Benefits Survey: Disability Benefits, Bureau of Labor Statistics website: *http://www.bls.gov/ebs2/chap3s.txt*, visited June 1, 1999.

[104] See Social Security Administration, *Social Security: Disability Benefits* (Washington, D.C.: Social Security Administration, 1996).

[105] See Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 281.

[106] See M. A. Rothstein, "Genetic Privacy and Confidentiality: Why They Are So Hard to Protect," *Journal of Law, Medicine and Ethics* 26 (1998): 198, 201. See also Rothstein, "Genetic Secrets: A Policy Framework," 474 ("The issues surrounding disability insurance are similar to those involved in life insurance, where the principal concern is balancing the risk of adverse selection against the desire to make available an important but not essential insurance product on an equitable basis.").

By contrast, the Council for Responsible Genetics argues that disability insurance is a basic good because it provides a "measure of economic security" following a disability. They contend that disability insurers should not be permitted to take genetic information into consideration in underwriting decisions.[107]

### *Long-Term Care Insurance*

Long-term term care insurance pays the costs of custodial and other extended care for persons who reside in nursing homes or at home.[108] While many people believe that private health insurance policies or Medicare will cover such care, that is generally not the case.[109]

Over 50 percent of long-term care expenses are paid by Medicaid, but in order to qualify for Medicaid, individuals must have no more than a few thousand dollars of assets, excluding certain items.[110] To reach this threshold, individuals must spend their assets on their care until they reach the Medicaid eligibility level.[111] Anticipating their future need for Medicaid and wishing to protect their assets, some individuals transfer their assets to others through sophisticated Medicaid estate planning years before they actually need long-term care, so that they will qualify for Medicaid if they need it.[112] Less than 5 percent of long-term care costs in the United States are paid by private long-term care insurance; the remainder of the costs are covered by Medicaid or paid for with personal assets.[113] In 1997, approximately 2.1 to 2.3 million elderly Americans had long-term care insurance and 7.3 million elderly Americans needed long-term care.[114]

In New York, the New York State Partnership for Long-Term Care has created incentives for New Yorkers to purchase private long-term care insurance.[115] New Yorkers

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[107] Council for Responsible Genetics, "Position Paper on Genetic Discrimination," Council for Responsible Genetics website: *http://www.gene-watch.org/gendisc.html*, visited June 1, 1999.

[108] Georgia State University, Department of Risk Management and Insurance, "Long Term Care Insurance Answers," Insweb website: *http://www.insweb.com/insurance101/qa/ltcare-a.htm*, visited June 2, 1999.

[109] Ibid.; M. Fogarty, "Genetic Testing, Alzheimer Disease, and Long-Term Care Insurance," *Genetic Testing* 3 (1999): 133, 134.

[110] See Fogarty, "Genetic Testing, Alzheimer Disease, and Long-Term Care Insurance," 134; J. L. Solterman, "Medicaid and the Middle Class: Should the Government Pay for Everyone's Long-Term Health Care?" *Elder Law Journal* 1 (1993): 251, 254–258; M. A. Cohen et al., "Financing Long-Term Care: A Practical Mix of Public and Private," *Journal of Health Politics, Policy and Law* 17 (1992): 403, 404.

[111] See Cohen et al., "Financing Long-Term Care," 404. This process is known as "spending down." Ibid.

[112] See Solterman, "Medicaid and the Middle Class," 265–273.

[113] See, e.g., Fogarty, "Genetic Testing, Alzheimer Disease, and Long-Term Care Insurance," 133–134. In addition, family members who provide long-term care to their relatives often incur hidden costs of leaving the workforce or taking time off work without pay. See ibid., 134.

[114] American Academy of Actuaries, "Long-Term Care: Actuarial Issues in Designing Voluntary Federal-Private LTC Insurance Programs," American Academy of Actuaries website: *ftp://www.actuary.org/monograf/ltc.pdf*, visited June 15, 2000.

[115] New York State Partnership for Long-Term Care, "About the NYSPLTC," New York State Partnership for Long-Term Care website: *http://www.nyspltc.org/about/index.html*, visited July 12, 1999.

who purchase long-term care insurance policies approved by the Partnership are automatically eligible for Medicaid long-term care benefits after the benefits of the private long-term care insurance policies expire, regardless of the level of their assets.[116]

Although few, if any, long-term care insurers now require applicants to take genetic tests, the situation may change if reliable genetic tests for diseases requiring extensive long-term care, such as late-onset Alzheimer disease, become available.[117] Currently, most long-term care insurers will not insure individuals who have long-term illnesses such as Alzheimer disease and diabetes.[118]

It is not clear whether the public considers long-term care to be an entitlement.[119] In discussing whether long-term care is a "basic human right," one commentator recognizes that a frequently cited reason for purchasing long-term care insurance is asset protection.[120] Nevertheless, she contends that long-term care insurance is not purchased simply to protect assets, but rather to help ameliorate the emotional and financial devastation caused by caring for a person with a long-term illness, to ensure that the beneficiary is able to afford a "quality nursing home," and to avoid the impoverishment of surviving spouses.[121]

Other commentators maintain that although many people do not currently regard long-term care as health care, American society will come to perceive it as such once the "baby boom" generation gets older and the need for long-term care grows.[122] This perception may lead individuals to conclude that long-term care should be made available to those who need it regardless of their genetic status and that, accordingly, long-term care insurers should be prohibited from underwriting based on genetic information.[123]

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[116] Ibid. The owners of these policies must, however, contribute their income for their long-term care after their policies have expired. See ibid.

[117] See generally Fogarty, "Genetic Testing, Alzheimer Disease, and Long-Term Care Insurance."

[118] B. S. Braun, "Long-Term Care and the Challenge of an Aging America: An Overview," *Quinnipiac Health Law Journal* 1 (1997): 113, 115.

[119] Fogarty, "Genetic Testing, Alzheimer Disease, and Long-Term Care Insurance," 136. See also Rothstein, "Genetic Privacy and Confidentiality," 201 (Public policy concerning the use of genetic information by long-term health insurers "depends to a large extent on whether long-term care is viewed more like health insurance or life (and disability) insurance").

[120] Ibid.

[121] Ibid.; see also Rothstein, "Genetic Privacy and Confidentiality," 201 (noting that the development public policy on the use of genetic information by long-term care insurers depends on whether it is viewed as a right to which all people should have access or as an "optional commercial transaction" in which "all parties may require any access to information deemed relevant").

[122] R. H. Binstock and T. H. Murray, "Genetics and Long-Term Care Insurance: Ethical and Policy Issues," in *Genetic Testing for Alzheimer Disease: Ethical and Clinical Issues*, ed. S. J. Post and P. J. Whitehouse (Baltimore: Johns Hopkins University Press, 1998), 155, 173–174. See also Rothstein, "Genetic Secrets: A Policy Framework," 474–475 (stating that, as with health insurers, long-term care insurers should not be permitted to require genetic testing for a "basic package" of long-term care). But see M. A. Rothstein, "Why Treating Genetic Information Separately Is a Bad Idea," *Texas Review of Law and Policy* 4 (1999): 33, 36–37 (stating that, as far as the use of genetic information for underwriting is concerned, long-term care insurance is somewhere "in-between" a societal right, such as health insurance, and an arm's-length commercial transaction such as life insurance and that, therefore, "our ultimate policy choice could go either way").

[123] Ibid., 174.

## The Use of Genetic Information by Employers

### Current Practice

Employers have generally collected medical information about employees and prospective employees for two purposes. One is to ensure that they hire only employees who will be healthy and productive workers. The second is to weed out individuals who are likely to make expensive claims on employer-provided health insurance and thereby raise costs.[124] Commentators and the public are concerned that employers will use genetic information for both of these reasons.[125]

The extent of employers' use of employees' genetic information to make adverse employment decisions is unclear.[126] A 1989 survey found that 15 percent of employers expected that, before the year 2000, they would check the genetic status of prospective employees and their dependents before making employment offers.[127] More recent surveys have found some anecdotal evidence of adverse employment actions based on

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[124] See M. A. Rothstein, "The Law of Medical and Genetic Privacy in the Workplace," in *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era* (New Haven, CT: Yale University Press, 1997), 281, 281–282; Kass, "The Implications of Genetic Testing for Health and Life Insurance," 309. Employers sometimes also collect health information on employees to protect the employee's health at the workplace. See, e.g., *Int'l Union United Autombile, Aerospace & Agricultural Implement Workers of America v. Johnson Controls, Inc.*, 499 U.S. 1871, 111 S. Ct. 1196 (1991) (employer refused to permit women of child-bearing age to work in a toxic environment that could harm fetuses). A discussion of the circumstances under which such collection and use of employees' health information by employers might be appropriate is beyond the scope of this report.

[125] See, e.g., P. S. Miller, "Genetic Discrimination in the Workplace," *Journal of Law, Medicine and Ethics* 26 (1998): 189, 189–190; K. H. Rothenberg et al., "Genetic Information and the Workplace: Legislative Approaches and Policy Challenges," *Science* 275 (1997): 1755, 1755; United States Department of Labor et al., "Genetic Information and the Workplace," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/HGP/Reports/ genetics_workplace.html*, visited February 22, 1999; Council for Responsible Genetics, "Position Paper on Genetic Discrimination," Council for Responsible Genetics website: *http://www.gene-watch.org/ gendisc.html*, visited June 1, 1999. Some employers might also desire to learn their employees' or potential employees' genetic information to determine whether the employees are especially susceptible to disease from exposure to workplace substances. Employers may also wish to monitor their employees for genetic mutations to determine whether workplace substances pose health hazards to their workforce. United States Department of Labor et al., "Genetic Information and the Work Place," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/HGP/Reports/ genetics_workplace.html*.

[126] To date, no controlled statistical studies have been performed on this issue. See Miller, "Genetic Discrimination in the Workplace," 190.

[127] Ibid.; United States Department of Labor et al., "Genetic Information and the Work Place," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/HGP/Reports/ genetics_workplace.html*.

individuals' genetic predispositions to disease.[128] However, some of these surveys have been criticized for using unrepresentative samples and drawing conclusions from the unverified beliefs of those surveyed about why adverse action was taken against them.[129] The 1999 American Management Association Survey on Workplace Testing found that less than 1 percent of the companies surveyed used predictive genetic test results to help make hiring, firing, or reassignment decisions, and approximately 5 percent used family history to make such decisions.[130]

Most commentators, including the AMA and the IOM Committee, agree that it is generally inappropriate for employers to fire, refuse to hire, or otherwise discriminate against qualified individuals in the terms and conditions of employment because they have genetic predispositions to disease.[131]

**Legal Considerations**

***Employee Retirement Income Security Act***

The Employee Retirement Income Security Act (ERISA) prohibits employers from firing or taking other adverse employment actions against employees in order to prevent them from claiming benefits under employee benefit plans.[132] Thus, under ERISA, an employer may not fire or otherwise discriminate against an employee with a genetic predisposition to disease because the employer anticipates that the employee will utilize employer-provided medical or other benefits.[133] Employers who do so are subject to civil lawsuits by the employees for back pay, front pay, medical benefits, and other equitable relief.[134]

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[128] United States Department of Labor et al., "Genetic Information and the Work Place," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/HGP/Reports/ genetics_workplace.html*.

[129] Miller, "Genetic Discrimination in the Workplace," 189 n.4; Health Insurance Association of America, "Genetic Testing: Media Kit," Health Insurance Association of America website: *http://www.hiaa.org/ newsroom/genetic.html*; S. M. Kopinsky, "Genetic Discrimination Is Less Widespread Than Feared," *The Health Care News Server* (November 20, 1997), Health Care News Server website: *http:// www.healthcarenewsserver.com/stories/HCN1997112000021.html*, visited June 30, 1999 (discussing comments by Dr. Philip Reilly and Dr. Dorothy Wertz).

[130] American Management Association, "1999 AMA Survey on Workplace Testing: Medical Testing," American Management Association website: *http://www.amanet.org/research/pdfs/wt99med.pdf*, visited October 20, 1999.

[131] See American Medical Association, Council on Ethical and Judicial Affairs, Genetic Testing by Employers § E-2.132; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 281–282; National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing in the United States*, ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of Health, 1997), 15.; United States Department of Labor et al., "Genetic Information and the Workplace," National Human Genome Research Institute website: *http:// www.nhgri.nih.gov/HGP/ Reports/genetics_workplace.html*.

[132] See 29 U.S.C.A. § 1140 (West 2000); *Morris v. Winnebago Indus., Inc.*, 936 F. Supp. 1509, 1520–1521 (N.D. Iowa 1996).

[133] See, e.g., *Folz v. Marriott Corp.*, 594 F. Supp. 1007 (W.D. Missouri 1984) (employer liable under ERISA for firing an employee with multiple sclerosis because of future health medical benefit claims employee might make).

[134] See, e.g., 29 U.S.C.A. 1132 (West 2000); *Schwartz v. Gregori*, 45 F.3d 1017 (6th Cir. 1995).

ERISA covers only existing employees; it provides no remedy to individuals who are denied employment because of concerns about health insurance costs.[135] Thus, ERISA does not prohibit employers from refusing to hire individuals with genetic predispositions to disease in order to save health insurance costs. In addition, individuals who claim that they have been discharged to prevent them from attaining a benefit under an employer benefit plan cannot recover under ERISA if the discharge was not motivated by an intent to interfere with the employee's right to benefits.[136] Thus, an employer who fires an employee with a genetic predisposition because the employer is concerned about diminished productivity would not be liable under ERISA.

### *Executive Order 13145*

On February 8, 2000, President Clinton issued Executive Order 13145, which prohibits discrimination in the terms and conditions of federal employment based upon an individual's "protected genetic information."[137] The law applies to employees, applicants for employment, and former employees.[138] Protected genetic information is defined as "information about an individual's genetic tests, information about the genetic tests of an individual's family members, or information about the occurrence of a disease or medical condition in family members of the individual."[139] The Executive Order prohibits the collection or disclosure of an employee's protected genetic information or information concerning the employee's receipt of or requests for genetic services.[140]

The Executive Order explicitly states that its purpose is to "clarify and make uniform administrative policy" and that it does not create any right or benefit that can be enforced in court.[141] Thus, unless the President enforces the Executive Order, federal employees who are victims of genetic discrimination by their employers will have no recourse to the Executive Order's provisions.[142]

### *New York Executive Law*

Section 296 of the New York Executive Law prohibits employers from discriminating against individuals in the terms and conditions of employment because of

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[135] J. Vogel, "Containing Medical and Disability Costs by Cutting Unhealthy Employees: Does Section 510 of ERISA Provide a Remedy?" *Notre Dame Law Review* 62 (1987): 1024, 1042–1043 & n.120.
[136] See *Schwartz v. Gregori*, 45 F.3d at 1021; *Humphreys v. Bellaire Corp*., 966 F.2d 1037, 1043 (6th Cir. 1992).
[137] Executive Order 13145 §§ 1-201, 1-202 (a),(b) (February 8, 2000).
[138] Ibid., § 1-201(a).
[139] Ibid., § 1-201(e)(1).
[140] Ibid., § 1-202(c),(d).
[141] Ibid., § 1-403.
[142] See, e.g., *Zhang v. Slattery*, 55 F.3d 732, 747–748 (2d Cir. 1995).

their "genetic predisposition or carrier status."[143] A genetic predisposition is "the presence of a variation in the composition of the genes of an individual which is scientifically or medically identifiable and which is determined to be associated with an increased statistical risk of being expressed as a physical or mental disease or disability in the individual but which has not resulted in any symptoms of such disease or disorder."[144] A carrier is "an individual who is at risk of having offspring with a genetically influenced disease but who has no predisposition on incurring the disease himself or herself."[145] Thus, under Section 296, it is unlawful to fire or to refuse to hire individuals who have genetic predispositions to breast cancer. In addition, Section 296 prohibits employers from refusing to hire individuals with genetic predispositions to breast cancer out of fear of higher insurance costs.[146]

Section 296 generally prohibits employers from requiring individuals to undergo genetic testing or to reveal genetic test results as a condition of employment[147] and forbids employers from even "mak[ing] an agreement with an individual to take a genetic test or to provide genetic test results."[148] In addition, Section 296 forbids employers from otherwise acquiring an individual's genetic test results or an interpretation of those results.[149] Employers who violate Section 296 are subject to liability for compensatory damages and other relief.[150]

Section 296 also prohibits employers from discriminating against individuals in the terms and conditions of employment on the basis of disability.[151] The term disability includes a physical, mental, or medical impairment that prevents the exercise of a normal bodily function.[152] The term also includes diagnosable medical anomalies that impair bodily integrity and do not prevent the exercise of normal bodily functions but may do so in the

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[143] N.Y. Exec. Law § 296(1)(a) (McKinney 1999). See also N.Y. Civ. Rights Law §§ 48-a, 48-b (McKinney 1999) (prohibiting employment discrimination against individuals who have "sickle cell trait" or are carriers of Tay-Sachs or Cooley's anemia).

[144] N.Y. Exec. Law § 292(21-b).

[145] Ibid., § 292(21-c). A genetic anomaly is "any variation in an individual's DNA which has been shown to confer a genetically influenced disease or predisposition to a genetically influenced disease or makes the individual a carrier of such variation." Ibid., § 292(21-a).

[146] See *State Div. of Human Rights v. Xerox Corp.*, 65 N.Y.2d 213, 218, 491 N.Y.S.2d 106, 108–09 (1985) (holding that under Section 296 "employment may not be denied because of any actual or perceived undesirable effect the person's employment may have on disability or life insurance programs"); *Antonsen v. Ward*, 77 N.Y.2d 506, 516, 569 N.Y.S.2d 328, 333 (1991) (same).

[147] N.Y. Exec. Law § 296(19)(a)(1) (McKinney 1999). Section 296 permits employers to require genetic testing as a condition of employment only "where such a test is shown to be directly related to the occupational environment, such that the employee or applicant with a particular genetic anomaly might be at an increased risk of disease as a result of working in said environment." Ibid., § 296(19)(b). A discussion of the circumstances under which such testing might be appropriate is beyond the scope of this report.

[148] Ibid., § 296(19)(a)(2).

[149] Ibid.

[150] Ibid., § 297(4), (9).

[151] Ibid., § 296(1)(a).

[152] See *State Division of Human Rights v. Xerox Corp.*, 65 N.Y.2d at 218–219, 491 N.Y.S.2d at 109; N.Y. Exec. Law § 292(21) (McKinney 1999).

future.[153] Under this latter definition of disability, the New York Court of Appeals has held that individuals with diagnosable but asymptomatic diseases are disabled.[154]

Since the integrity of the genetic structure of a cell with a genetic mutation may arguably be said to be impaired, an asymptomatic genetic mutation may qualify as a disability under Section 296. If so, asymptomatic individuals with genetic predispositions to disease would be protected from discrimination in the terms and conditions of employment under the disability provisions of Section 296, as well as the provisions that specifically address genetic discrimination. The disability provisions also would protect individuals who are discriminated against because of a mistaken perception that they have a genetic predisposition to disease; [155] this protection does not exist under the genetic discrimination provisions of section 296.[156]

## The Impact of the Americans with Disabilities Act

Besides the limited protections of HIPAA and Executive Order 13145,[157] no federal law expressly prohibits discrimination against individuals based on their genetic predisposition to disease or their carrier status.[158] However, some commentators have argued that the Americans with Disabilities Act (ADA) can be interpreted to prohibit such discrimination.[159] A broad interpretation of the ADA in this area could significantly affect many of the legal principles discussed above.

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[153] See *State Division of Human Rights v. Xerox Corp.*, 65 N.Y.2d at 218–219, 491 N.Y.S.2d at 109.

[154] See *Antonsen v. Ward*, 77 N.Y.2d 506, 510–511, 513, 569 N.Y.S.2d 328, 329–331 (1991) (asymptomatic Crohn's disease is a disability within the meaning of Section 296); *State Division of Human Rights v. Granelle*, 70 N.Y.2d 100, 517 N.Y.S.2d 715 (1987) (asymptomatic spondylolisthesis is a disability within the meaning of Section 296).

[155] See N.Y. Exec. Law §§ 292(21)(c), 296(1)(a) (McKinney 1999) (prohibiting employment discrimination against persons perceived as having a disability); *Ashker v. International Bus. Machs. Corp.*, 168 A.D.2d 724, 726, 563 N.Y.S.2d 572, 574 (N.Y. App. Div. 1990) (same); *Doe v. Roe*, 160 A.D.2d 255, 255–256, 553 N.Y.S.2d 364, 364–365 (N.Y. App. Div. 1990); *Romei v. Shell Oil Co.*, 1991 WL 692884 (Sup. Ct. N.Y. Cty. 1991). See also *Matter of North Shore Univ. Hosp. v. Rosa*, 86 N.Y.2d 413, 633 N.Y.S.2d 462 (1995) (implicitly recognizing that the definition of disability within the meaning of section 296 includes being perceived as disabled).

[156] In addition, the provisions of Section 296 that prohibit housing discrimination, discrimination in public accommodations, and other forms of discrimination against individuals with disabilities would also cover individuals with asymptomatic genetic predispositions to disease.

[157] See pages 286, 289, 297, this chapter.

[158] See Miller, "Genetic Discrimination in the Workplace," 189.

[159] Ibid., 191.

### Is Asymptomatic Genetic Predisposition to Disease or Genetic Carrier Status a Disability under the ADA?

The ADA prohibits employers and places of public accommodation[160] from discriminating against individuals with disabilities.[161] It defines disability as (1) "a physical or mental impairment that substantially limits one or more of the major life activities," (2) "a record of such an impairment," or (3) "being regarded as having such an impairment."[162]

The ADA clearly protects individuals who currently have genetic conditions that are symptomatic and that substantially limit major life activities, as well as individuals who have a record of or are regarded as having such conditions.[163] However, no court has ruled on whether an asymptomatic individual who has a genetic predisposition to disease, but who does not currently suffer from the disease, or an individual who is a carrier of a genetic disease that may affect his or her offspring, has an "impairment" that "substantially limits major life activities" within the meaning of the ADA.[164]

Under the ADA, the term "impairment" includes physiological disorders that adversely affect various body systems such as the respiratory, cardiovascular, and neurological systems.[165] Thus, in order to qualify as "impairments," asymptomatic genetic predispositions to disease and genetic carrier status would have to adversely affect a body system. It may be difficult to establish that predispositions to disease and genetic carrier status, in and of themselves, satisfy this requirement. For example, single mutations in one of the two copies of the BRCA1 and APC genes, which may indicate predispositions to breast cancer and colon cancer, respectively, do not by themselves adversely affect body systems.[166] They generally begin to adversely affect body systems only if BRCA1 and APC mutations also arise in the second copy of an individual's genes.[167] The Equal Employment Opportunity Commission (EEOC), the federal agency charged with implementing the employment provisions of the ADA, has opined that a mere

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[160] The ADA includes a list of places that are considered public accommodations. 42 U.S.C.A. § 12181(7)(West 2000). For example, public accommodations include inns, restaurants, and theaters. Ibid., § 12181(7) (a), (b), (c).

[161] 42 U.S.C.A. §§ 12112(a) (employment), 12182(a) (public accommodations) (West 1999).

[162] Ibid., § 12102(2)(A), (2)(B), (2)(C). An employer or public accommodation "regards" an individual as disabled within the meaning of the ADA if it mistakenly believes that (1) the individual has an impairment and (2) that the impairment substantially limits the individual's ability to currently perform a major life activity. See, e.g., *Sutton v. United Airlines, Inc.*, 527 U.S. 471, ___, 119 S. Ct. 2139, 2150 (1999); *Reeves v. Johnson Controls World Servs.*, 140 F.3d 144, 153–154 (2d Cir. 1998).

[163] See Miller, "Genetic Discrimination in the Workplace," 190.

[164] Ibid. While not ruling on the issue, at least three justices of the Supreme Court, Chief Justice Rehnquist and Justices Thomas and Scalia, have recognized the possibility that individuals with "genetic markers" might attempt to make claims under the ADA in the future. See *Bragdon v. Abbott*, 524 U.S. at 661, 118 S. Ct. at 2216 (Rehnquist, C.J., dissenting).

[165] See *Bragdon v. Abbott*, 524 U.S. at 632, 118 S. Ct. at 2202–2205.

[166] For a discussion of BRCA and APC gene mutations, see Chapter 2, pages 36, 38, 42; Chapter 3, page 63.

[167] Telephone interview with Dr. Harry Ostrer, Director, Human Genetics Program, Department of Pediatrics, New York University School of Medicine, April 18, 1999.

"predisposition to an illness or disease does not qualify as an impairment" within the meaning of the ADA.[168]

Even assuming that an asymptomatic genetic disorder constitutes an "impairment" within the meaning of the ADA, it would still be necessary to show that it substantially limits a major life activity. Major life activities include walking, seeing, hearing, speaking, breathing, and reproduction. [169] The Supreme Court has recently made clear that the impairment must substantially limit a major life activity *currently*, not at some point in the future, in order to qualify as a disability.[170] Thus, the fact that an asymptomatic person with a BRCA1 gene mutation might develop breast cancer in the future would probably be insufficient, in itself, to qualify the mutation as a "disability." In addition, carriers of recessive genetic diseases, such as cystic fibrosis, will never develop the disease, and thus their carrier status is also insufficient to qualify as a disability.

Some commentators have suggested that asymptomatic individuals with genetic predispositions to disease might be substantially limited in the major life activity of reproduction.[171] In *Bragdon v. Abbott*,[172] the Supreme Court ruled that individuals who are HIV positive are substantially limited in the major life activity of reproduction because of the likelihood that they will transmit HIV to their offspring. In the genetics context, it might be argued that individuals at risk of transmitting a genetic disease, or a genetic predisposition to a late-onset disorder, are disabled because they are substantially limited in the major life activity of reproduction. Even if this argument is accepted, however, it is unlikely that courts would conclude that *all* genetic predispositions or traits constitute disabilities within the meaning of the ADA. In the HIV context, the Supreme Court concluded that the possibility of transmitting HIV impedes reproduction because AIDS is "a dread and fatal disease" and the likelihood of a woman transmitting HIV to her child is at least 8 percent.[173] For individuals with genetic predispositions to less serious disorders or disorders that occur late in life, or in cases where the trait has only a remote chance of resulting in a disease in the individual's offspring,[174] courts might be

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[168] *Cornman v. N.P. Dodge Management Co.*, 43 F. Supp.2d 1066, 1071 (D. Minn. 1999); 29 C.F.R. § 1630.2(h) Appendix (1999). See also W. E. Parmet, "The Supreme Court Confronts HIV: Reflections on Bragdon v. Abbott," *Journal of Law, Medicine and Ethics* 26 (1998): 225, 236 (suggesting that "genetic carriers" do not necessarily have impairments within the meaning of the ADA).

[169] See *Bragdon v. Abbott*, 524 U.S. at 636–637, 118 S. Ct. at 2204–2205; 29 C.F.R. § 1630.2(i) (1999) (interpretation of the phrase "major life activities" by the Equal Opportunity Employment Commission (EEOC)). The Supreme Court has not yet ruled on what deference, if any, is due to the EEOC's interpretation of the ADA. See *Sutton v. United Airlines, Inc.* e.g., 527 U.S. at ___, 119 S. Ct. at 2145.

[170] See, e.g., *Sutton v. United Airlines, Inc.*, 527 U.S. at ___,119 S. Ct. at 2146.

[171] See Parmet, "The Supreme Court Confronts HIV," 236; Rothstein, "Genetic Privacy and Confidentiality," 202 n.21.

[172] 524 U.S. 624, 118 S. Ct. 2196 (1998).

[173] Ibid.

[174] For a discussion of the "penetrance" of different genetic mutations, see Chapter 1, page 13.

less willing to conclude that the likelihood of transmission impedes the ability to reproduce.[175]

Another way to fit persons with genetic predispositions to disease or persons who are carriers for genetic disorders into the scope of the ADA is to argue that these persons are "regarded" as having impairments that substantially limit major life activities. The EEOC has opined that employers who discriminate in the terms and conditions of employment against asymptomatic individuals with genetic predispositions to disease, because of concerns about their future insurance costs or diminished productivity, violate the ADA. The EEOC contends that such actions indicate that the employers are "regarding" the individuals as having an impairment that substantially limits a major life activity.[176] However, it is not clear whether this interpretation will be upheld by the courts. A recent decision by the Supreme Court has made clear that to "regard" an individual as disabled, an employer must believe that the employee has an impairment that *currently* limits a major life activity.[177] An employer who discriminates against individuals with genetic predispositions to disease based on concerns about future insurance costs or diminished productivity does not necessarily regard the individual as currently limited in a major life activity.[178]

**The ADA and Insurance**

Most courts have ruled that the ADA prohibits employers and insurers from refusing to offer persons with disabilities the same insurance packages they offer to persons without disabilities,[179] unless the insurers can show that their actions are based on, or not inconsistent with, state laws and are not a "subterfuge" to evade the purposes of the ADA.[180] For example, an insurance company that sells a health insurance package

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[175] See Parmet, "The Supreme Court Confronts HIV," 236.

[176] See Equal Employment Opportunity Commission, *EEOC Compliance Manual* vol. 2 (CCH) § 902 (Mar. 14, 1995).

[177] See, e.g., *Sutton v. United Airlines, Inc.*, 537 U.S. at ___, 119 S. Ct. at 2146, 2149–2150.

[178] Cf. ibid. (the fact that an airline refused to hire individuals with poor eyesight did not alone prove that the employer regarded the individuals' poor eyesight as "substantially limiting" the major life activity of working; it proved only that the airline believed that the individuals' poor eyesight precluded them from working as airline pilots); *Reeves v. Johnson Controls World Servs.*, 140 F.3d at 153–154 (employees must show not only that their employers took adverse employment action against them because the employers regarded them as impaired, but also that the employer believed that the impairment substantially limited a major life activity).

[179] See, e.g., *Pallozzi v. Allstate Life Ins. Co.*, 198 F.3d at 31–32; *Doe v. Mutual of Omaha Ins. Co.*, 179 F.3d 557, 561, 563–564 (7th Cir. 1999); *Ford v. Schering Plough Corp.*, 145 F.3d 601, 608 (3rd Cir. 1998). Courts have ruled that the ADA's protections against disability discrimination apply to individuals who purchase insurance directly from insurers, see, e.g., *Pallozzi*, 198 F.3d at 31–33; *Doe v. Mutual of Omaha Ins. Co.*, 179 F.3d at 559, or who obtain insurance through their employer-sponsored plans. See, e.g., *McNeil v. Time Ins. Co.*, 205 F.3d 179, 186–189 (5th Cir. 2000) (describing circumstances under which an employee's challenge to employer-provided group insurance policy could prevail under the ADA); *Parker v. Metropolitan Life Ins. Co.*, 121 F.3d 1006, 1014–1015 (6th Cir. 1997) (en banc), *cert. denied*, 522 U.S. 1084, 118 S. Ct. 871 (1998).

[180] See *Pallozzi v. Allstate Life Ins. Co.*, 198 F.3d at 31–33. Because self-insured employers are not subject to state insurance laws, see 29 U.S.C.A. § 1144 (a), (b)(2)(B) (West 2000), they are required to establish

that includes asthma coverage would most likely be prohibited from excluding asthma coverage from policies offered to persons who are deaf. Accordingly, if asymptomatic individuals with genetic predispositions to disease are considered disabled within the meaning of the ADA, courts will likely agree that, absent state law justifications, employers and insurers may not refuse to offer them the same insurance packages they offer to individuals without disabilities.[181]

However, most courts agree that the ADA does not require insurers or employers to provide insurance that covers all disabilities equally or that covers particular disabilities. For example, courts have held that, even without an underwriting basis, employers and insurers may refuse to provide the same level of coverage for mental and physical disabilities.[182] Under this reasoning, the ADA would permit employers and insurers to refuse to cover or to limit coverage for specific genetic diseases, such as Huntington disease and cystic fibrosis, without any underwriting justification for doing so.

**The ADA and Employment**

If courts consider asymptomatic individuals who have genetic predispositions to disease disabled within the meaning of the ADA,[183] employers would be prohibited from taking adverse employment actions against them based on these predispositions, assuming the individuals are otherwise qualified for the job.[184] Even if courts do not rule that asymptomatic individuals with genetic predispositions to disease are disabled within the meaning of the ADA, the ADA would still prohibit employers from taking adverse

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only that their activities are not a subterfuge to evade the purposes of the ADA. See 42 U.S.C.A. § 12201 (c)(3) (West 2000); *EEOC v. Aramark Corp.*, 208 F.3d 266, 269 (D.C. Cir. 2000); *Krauel v. Iowa Methodist Med. Ctr.*, 95 F.3d 674, 678 (8th Cir. 1996). A "subterfuge" includes "a specific intent to circumvent or evade the statutory purpose" of the ADA. *EEOC v. Aramark Corp.*, 208 F.3d at 269; *Leonard F. v. Israel Discount Bank of New York*, 199 F.3d 99, 102–104 (2d Cir. 1999). See also *Krauel v. Iowa Methodist Med. Ctr*, 95 F.3d at 678–679 (an employment "benefit plan cannot be a subterfuge unless the employer intended by virtue of the plan to discriminate in a non-fringe-benefit-related aspect of the employment relation").

[181] See page 300, this chapter.

[182] See, e.g., *E.E.O.C v. Staten Island Savings Bank*, ___ F.3d ___, 2000 WL 297510, *4 (2d Cir. 2000); *Weyer v. Twentieth Century Fox Film Corp.*, 198 F.3d 1104, 1116–1118 (9th Cir. 2000); *Kimber v. Thiokol Corp.*, 196 F.3d 1092, 1101–1102 (10th Cir. 1999); *Lewis v. Kmart Corp.*, 180 F.3d 166, 170 (4th Cir. 1999), *cert. denied*, ___ U.S. ___, 120 S. Ct. 978 (2000); *Ford v. Schering-Plough Corp.*, 145 F.3d 601, 608–612 (3rd Cir.1998), *cert. denied*, __ U.S. __, 119 S. Ct. 850 (1999); *Parker v. Metropolitan Life Ins. Co.*, 121 F.3d at 1012; *EEOC v. CNA Ins. Co.*, 96 F.2d 1039, 1044–1045 (7th Cir. 1996). Cf. *Modderno v. King*, 82 F.3d 1059, 1060–1065 (D.C. Cir. 1996) (disparate treatment of mental and physical disability permissible under the federal Rehabilitation Act, a statute analogous to the ADA).

[183] See page 300, this chapter.

[184] See 42 U.S.C.A. 11213(a) (West 2000).

employment actions against them as a result of regarding them as having a disability.[185] Thus, for example, if an employer were to fire or refuse to hire an asymptomatic individual with the genetic mutation that causes Huntington disease because the employer mistakenly believes that the mutation substantially and presently interferes with the employee's ability to think rationally, the employer will have violated the ADA and can be held liable for compensatory and punitive damages.[186]

The ADA prohibits employers from performing medical examinations on or asking disability-related questions of job applicants prior to extending to them a conditional offer of employment.[187] Disability-related questions include "any question that is likely to elicit information about a disability," and for all practical purposes encompass almost all medical questions.[188] A conditional offer of employment is a bona fide job offer that is subject only to the results of subsequent medical inquiries and/or medical examinations of the applicant.[189] Even after making a conditional offer of employment, an employer may only make such inquiries or conduct such examinations if it does so for all of the other applicants for the job in question. The ADA does not limit the scope of the inquiries and the examinations.[190]

After an individual has been hired as an employee, the employer may conduct medical examinations of the employee or ask the employee medical questions only if the examinations and/or inquiries are "job-related" and "consistent with business necessity."[191] For example, an employer may require a warehouse laborer to undergo a medical examination by an orthopedist if the laborer's back impairment is interfering with his job performance.[192]

Courts are divided about whether job applicants and employees who do not have disabilities may make claims under the ADA against employers for making improper medical inquiries or improperly requiring medical examinations.[193] No court has ruled on

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[185] See page 300, this chapter.
[186] See 42 U.S.C.A. 11217(a) (West 2000).
[187] See T. L. Clark, "A Map for the Labyrinth: How to Conduct Job Interviews and Obtain Medical Information without Violating the Americans with Disabilities Act," *Labor Lawyer* 13 (1997): 121, 123.
[188] Ibid., 123–131 (internal quotation marks omitted).
[189] Ibid., 134.
[190] Ibid., 135.
[191] 42 U.S.C.A §12112(d)(4)(A) (West 2000).
[192] Equal Employment Opportunity Commission, *EEOC Compliance Manual: A Technical Assistance Manual on the Employment Provisions of (Title I) of the Americans with Disabilities Act*, Chap. VI., Medical Examinations and Inquiries § 6.6 (Washington, D.C.: Equal Employment Opportunity Commission, 1992).
[193] Compare, e.g., *Fredenburg v. Contra Costa County Dep't of Health Servs*, 172 F.3d 1176, 1181–1182 (9th Cir. 1999) (nondisabled individuals may sue employers under the ADA for improper medical examinations and inquiries); *Griffin v. Steeltek, Inc.*, 160 F.3d 591, 593–595 (10th Cir. 1998) (same), *cert. denied*, ___ U.S.___, 119 S. Ct. 1455 (1999), with *Armstrong v. Turner Indus., Ltd.*, 950 F. Supp. 162, 166–168 (M.D. La. 1996) (nondisabled individuals may not sue), *aff'd on other grounds*, 114 F.3d 554 (5th Cir. 1998); *Varnagis v. City of Chicago*, 1997 WL 361150,*7 (N.D. Ill. 1997). See also *Cossette v. Minnesota Power & Light*, 188 F.3d 964, 969–970 (8th Cir. 1999) ("a plaintiff need not be disabled to state a claim [under the ADA] for the unauthorized gathering or disclosure of confidential medical information").

the extent to which the ADA constrains employers' ability to ask job applicants about their genetic predispositions to disease or to require them to take genetic tests.

## Conclusions and Recommendations

### Health Insurance and Individual Medical Underwriting

**Access to health care is a necessity for all Americans, and for most Americans, health insurance provides such access. By limiting individual medical underwriting in health insurance, New York's community rating and open enrollment laws appropriately seek to make access to medical care more equitable.**

Health care is a necessity for everyone throughout their lives, and most Americans obtain health care by using some form of health insurance. However, approximately 40 million Americans do not have any health insurance at all. One of the factors that makes it difficult for some people to obtain health insurance is medical underwriting. In many states, insurers that sell individual health insurance policies can, and do, use medical underwriting to charge certain individuals higher premiums or to refuse them coverage altogether.

In light of the fundamental importance of health care to all individuals, we believe that access to health insurance should not be denied because of a person's medical history or current medical condition. While many of us advocate the development of a national universal health care system, we recognize that such a system is not likely to be created in the near future. In the meantime, prohibitions on individual medical underwriting for individual and small group health insurance policies, combined with community rating and open enrollment, are one way to attempt to make access to health care more equitable. Accordingly, we support New York's community rating and open enrollment laws and urge their continuance.

### Current Protections against Adverse Insurance Decisions by Health Insurers Based on Genetic Information

**The combination of New York and federal laws currently protects New Yorkers from adverse insurance decisions by health insurers based on genetic information.**

Taken together, New York and federal law provides significant protections to New Yorkers against adverse insurance decisions by health insurers based on genetic information. For individual and small group health insurance policies, the community

rating and open enrollment laws effectively preclude the use of genetic information in coverage and premium decisions. New York law also prohibits individual and small group health insurers from treating genetic information as a pre-existing condition.[194] For group health plans, New York and federal laws prohibit insurers and employers from charging higher premiums or refusing to provide coverage for an individual based on the individual's health status, medical history, or genetic information.[195] The law also prohibits group health plans from treating genetic information as a pre-existing condition.[196] As a result of these protections, it is not necessary to consider legislation prohibiting the use of genetic information in health insurance in New York State.

**Use of Genetic Test Results by Life, Disability, and Long-Term Care Insurers**

> **New York insurance law should be amended to require a moratorium on requests for genetic test results and the use of genetic test results in underwriting, by life, disability, and long-term care insurers. Insurers should be permitted to use these results for underwriting only when (1) the subjects of the tests voluntarily provide the results to the insurer and (2) the insurers will use the results for the subjects' benefit.**

The use of genetic information in life, disability, and long-term care insurance raises different public policy issues than the use of genetic information in health insurance. Except for the extremely wealthy, health insurance is necessary to obtain access to basic medical care; individuals who cannot obtain private insurance and who do not qualify for public programs such as Medicaid generally lack access to all medical care except in emergencies. The primary goal of life, disability, and long-term care insurance, by contrast, is the preservation of financial assets in the event of death, disability, or long-term illness.[197] Access to strategies for building financial assets is not generally considered as basic a need as access to medical care.

In light of this distinction, the fact that health insurance is available in New York State without medical underwriting does not necessarily mean that life, disability, and long-term care insurers should be prohibited from engaging in medical underwriting as well. While there are strong arguments for enabling individuals to obtain at least basic life, disability, and long-term care insurance policies without regard to medical risk,[198]

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[194] See page 287, this chapter.
[195] See page 289, this chapter.
[196] See page 289, this chapter.
[197] This is true even for long-term care insurance. Because Medicaid will pay for the long-term care needs of most individuals whose assets fall below a certain level, see page 293, this chapter, private long-term care insurance is generally not necessary to obtain access to long-term care.
[198] For many Task Force members, this argument is most compelling in the context of long-term care. While the Medicaid program provides access to long-term care for those individuals who qualify, it does not necessarily provide access to the highest quality long-term care services. See Fogarty, "Genetic Testing, Alzheimer Disease, and Long-Term Care Insurance," 136. In addition, many Task Force members are troubled by a system that requires individuals to become impoverished as a condition of obtaining care.

there are countervailing considerations, particularly those related to adverse selection. Ultimately, the design of equitable and cost-effective systems of life, disability, and long-term care insurance raises a host of complex issues outside the scope of this report.

Nevertheless, regardless of the appropriateness of medical underwriting in life, disability, and long-term care insurance as a general matter, the Task Force agrees that, at the present time, a moratorium should be placed on underwriting *based on the results of genetic tests*.[199]

First, evidence indicates that a significant percentage of individuals have refused or will refuse to undergo genetic testing out of fear that the results could be used against them by insurers. This is true in both the treatment and medical research contexts.[200] We are concerned that this fear will continue to inhibit individuals from participating in genetic research and from undergoing genetic tests that are necessary for their own health.

Second, rapid developments in genetic research have lead to frequent re-evaluations of the predictive value of many genetic tests. Because of this, actuarial calculations made by insurers regarding individuals who test positive for a genetic predisposition to disease may be inaccurate as soon as, or soon after, insurers calculate them. Improper raising of premium rates by life insurers based on sickle cell carrier status in the early 1970s suggests that insurers may be all too willing to use genetic test results for medical underwriting without sufficient justification.[201] Accordingly, at least at present, life, disability, and long-term care insurers should not be permitted to use genetic test results to make adverse insurance decisions.

Third, underwriting based on genetic test results is particularly unfair because, given the nascent state of genetics knowledge, its effect will be to deny access only to those individuals unfortunate enough to have the specific genetic mutations that researchers have already identified. Virtually all individuals have genetic mutations that predispose them to some disorder or disease; the fact that tests are not yet available to detect these mutations does not mean that these individuals are genetically "healthier" than persons who have mutations for which tests currently exist. Moreover, many of those individuals who have genetic mutations for which testing is now available (and who might be precluded from purchasing affordable life, disability, or long-term care insurance as a result) are members of racial or ethnic minority groups. This is true because genetic research is easier to perform in relatively homogeneous populations, so

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[199] We recognize that, because of ERISA, any amendments to New York State's insurance laws about the use of genetic information by insurers will not apply to employers who are self-insured. See note 180, above. Accordingly, we urge the federal government to consider similar limitations on the use of genetic information in insurance underwriting as a matter of federal law.

[200] See pages 282–283, this chapter; Chapter 7, page 188.

[201] See page 281, this chapter.

researchers typically target groups, such as Ashkenazi Jews, where shared genetic variations are more easily found. As a result, allowing insurers to use the results of currently available genetic tests in underwriting decisions may have a disparate impact on minority populations, which public policy should take steps to prevent.

Finally, insurers claim that they are not currently using genetic test results in underwriting because the tests are expensive and reveal only a limited number of serious genetic abnormalities.[202] Thus, prohibiting insurers from using these results should not interfere with their current underwriting practices and financial stability and should not lead to adverse selection.[203] In addition, there is no evidence, of which we are aware, that adverse selection has occurred in states that prohibit insurers from using genetic test results in underwriting, and there is little indication that adverse selection has occurred as a result of other underwriting prohibitions.[204]

We recognize that there exist genetic mutations, such as the mutation that causes Huntington disease, that are highly penetrant and predictive. However, the vast majority of persons with such mutations will have family histories of the diseases with which the mutations are associated.[205] Because life, disability, and long-term care insurers generally have access to family medical histories, the effect of a moratorium on insurance underwriting using genetic test results should be minimal.

However, insurers should be permitted to use genetic test results for a subject's benefit if, without a request from the insurer, the subject voluntarily submits the results to the insurer. For example, it should be permissible for an individual with a family history of Huntington disease to submit a negative test result to a disability insurer to obtain lower rates for the insurance.

### Use of Genetic Information by Employers

**New York Law provides significant protections against adverse use of genetic information by employers. As a result of these protections, it is not necessary to consider further legislation in New York prohibiting the use of genetic information by employers.**

New York law prohibits employers from discriminating against individuals in the terms and conditions of employment because of their genetic predisposition or carrier status[206] and forbids employers from requiring individuals to undergo genetic testing or to reveal genetic test results as a condition of employment. Employers who violate these

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[202] Ibid.
[203] See page 284, this chapter (discussing adverse selection).
[204] See page 285, this chapter.
[205] See Chapter 3.
[206] Individuals who show symptoms of genetic diseases are protected from employment discrimination by New York's prohibition against disability discrimination in employment. See page 298, this chapter.

prohibitions can be sued by the individuals whom they have wronged.[207] We support these protections and hope that they will serve as a model for other states and the federal government.

# 11

# Public Health Role in Genetic Services

## Overview of Public Health

Whereas clinical medical practice focuses on individual patients, public health focuses on disease prevention for whole populations and promotion of "healthful conditions for the community at large."[1] Public health activities are overseen largely by governmental agencies, often working in concert with clinics, academic institutions, and community-based organizations. Public health professionals include physicians, nurses, laboratory scientists, social workers, health educators, sanitarians, and administrators.

### History

Organized public health activities in the United States began in the eighteenth century and focused on prevention of infectious diseases, including tuberculosis, smallpox, cholera, and typhoid fever, many of which were linked to increased urbanization. Public health agencies, appearing by the mid- to late-1800s, ensured clean and safe water supplies and undertook other measures, such as quarantine of infected individuals, to limit the spread of communicable diseases.[2] By 1900, the establishment of the science of bacteriology provided the basis for public health training of individuals with a special area of expertise.[3]

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[207] Ibid.

[1] R. D. Lasker and the Committee on Medicine and Public Health, *Medicine and Public Health: The Power of Collaboration* (New York: New York Academy of Medicine, 1997), 3.

[2] Committee for the Study of the Future of Public Health, Division of Health Care Services, Institute of Medicine, *The Future of Public Health* (Washington, D.C.: National Academy Press, 1988), 56–62; Lasker, *Medicine and Public Health*, 12.

[3] Lasker, *Medicine and Public Health*, 14; Institute of Medicine Committee for the Study of the Future of Public Health, *The Future of Public Health*, 63–65.

Commentators cite public health activities as a significant factor in this century's increase in average life expectancy for Americans from about forty-five to seventy-five years.[4]

In the latter half of the twentieth century, the discovery and implementation of antibiotics and other lifesaving medical interventions and drugs shifted the groundwork of public health activities. Medicine and public health, previously meshed, diverged. Medicine, based in the biological and chemical sciences, generally was practiced on a fee-for-service basis that was organized for treatment of individual patients. Public health, grounded in the population-based sciences of epidemiology[5] and biostatistics and in preventive approaches to community health, generally became the domain of governmental agencies.[6] "New" public health, while still ensuring sanitary practices to prevent communicable diseases, gradually widened its focus to include activities such as maternal and child health and preventive health education.[7]

**Governmental Agencies**

Public health agencies exist on federal, state, and local levels. Historically, state and local health agencies were established first; forty states established health agencies by 1900.[8] The state agencies were and remain the locus of many public health activities. Federal activities, principally located in the United States Public Health Service,[9] followed and have expanded throughout the twentieth century. The federal government establishes standards, policies, and regulations; conducts research and disseminates research findings; supports state and local public health activities; ensures equity across states; develops national priorities; and responds to international health threats.[10] Since the 1960s, the federal role in ensuring public health has extended to include the Medicare and Medicaid programs, which support expanded direct patient health services to the elderly, disabled, and other vulnerable populations.[11]

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[4] See, e.g., B. R. Bloom, "The Future of Public Health," *Nature* 402 suppl. (1999): C63.

[5] Epidemiology is "the study of the distribution and determinants of disease frequency" in human populations. See C. H. Hennekens and S. L. Mayrent, *Epidemiology in Medicine* (Boston: Little, Brown and Company, 1987), 3.

[6] Lasker, *Medicine and Public Health*, 21.

[7] Ibid., 15.

[8] The first established governmental health agency was the New York City Department of Health, established in 1866. Institute of Medicine Committee for the Study of the Future of Public Health, *The Future of Public Health*, 61.

[9] For an overview of the Public Health Services agencies and activities, see ibid.; see also J. K. Ingelhart, "Health Policy Report: Politics and Public Health," *New England Journal of Medicine* 334 (1996): 203. Agencies include the Food and Drug Administration, the National Institutes of Health, and the Centers for Disease Control and Prevention.

[10] Institute of Medicine Committee for the Study of the Future of Public Health, *The Future of Public Health*, 68; American Public Health Association, "The Role of Public Health in Ensuring Healthy Communities," *American Journal of Public Health* 86 (1994): 448, 450.

[11] Institute of Medicine Committee for the Study of the Future of Public Health, *The Future of Public Health*, 69. The Medicare and Medicaid programs were established as Titles 18 and 19 of the 1966 Social Security Act.

**Public Health Mission: The Institute of Medicine Report**

In the late 1980s, the Institute of Medicine, citing concern that the nation had lost consensus about the roles and responsibilities of public health, formed a committee to reassess the mission of public health. The Committee for the Study of the Future of Public Health issued its report in 1988, affirming the importance of public health activities, which it defined as "organized community efforts aimed at the prevention of disease and the promotion of health."[12] It defined public health's mission as "fulfilling society's interest in assuring conditions in which people can be healthy" through the application of scientific and technical knowledge.[13]

The Committee outlined three core functions by which public health agencies fulfill this mission: assessment, policy development, and assurance.[14] Assessment activities include the systematic collection, assembly, analysis, and dissemination of information about the health of a community, including population statistics and epidemiologic data. This information is critical to policy development, which entails a wide range of interactions among government health officials and other public and private organizations and individuals. This function includes planning, policy setting, advocacy, and provision of public information to help communities make informed decisions. The final function, assurance, is based on health agencies' authority to oversee the provision of safe and reliable services to community members. It includes assurance of access to health services, training of medical and health professionals, and oversight of clinical laboratories. It also includes enforcement of laws and regulations to reduce community health risks, for example, water quality control and lead abatement.

In its conclusions and recommendations, the Committee found that states "are and must be the central force in public health."[15] The Committee called on states to reassess their public health assessment, policy, and assurance activities and to "support a set of modern disease control measures that address contemporary health problems," including AIDS, cancer, and heart disease.[16] They also acknowledged the important role of the federal government in support of development and dissemination of health information, establishment of nationwide priorities and objectives, and support of state and local agencies.[17]

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[12] Ibid., 41.
[13] Ibid., 7, 40.
[14] Ibid., 43–45.
[15] Ibid., 8.
[16] Ibid., 8, 146.
[17] Ibid., 9.

## Traditional Public Health Genetic Services

Historically, public health genetic services have focused on single-gene diseases[18] and congenital malformations.[19] In the United States, such disorders affect 2 to 4 percent of births and account for approximately one-third of childhood tertiary care hospitalizations.[20]

Public health genetic services have aimed to prevent disease-associated morbidity and mortality at three levels: primary, secondary, and tertiary.[21] Primary prevention refers to preventing disease morbidity and mortality before it happens. One example is public health educational campaigns to promote the reduction of births affected by neural tube defects by maternal supplementation of the B vitamin folic acid before conception and in the early stages of pregnancy.[22] Secondary preventive measures aim to prevent future morbidity in those diagnosed as having a disease or disorder; newborn screening is a secondary preventive measure.[23] Tertiary prevention aims at minimizing pre-existing symptoms. Tertiary prevention is more in the realm of clinical medical care, where diagnostic genetic testing, among other forms of diagnostic testing, may help lead to an appropriate diagnosis and medical care plan. Public health efforts in tertiary prevention include efforts to ensure access to medical services, for example, therapy to minimize the morbidity and pain of sickle cell disease episodes.

### *State Activities*

State health agencies are the locus of genetic public health services to the public. The traditional focus of state agencies has been congenital disorders and single-gene diseases, through programs such as newborn screening,[24] surveillance for congenital anomalies (e.g., by state registries), and assurance of access to clinical genetic services for

[18] Single-gene diseases are diseases that result from inheritance of a mutant variant of a single gene or single pair of genes. See Chapter 1, page 14.

[19] Congenital malformations are structural or physiological defects present at birth which may be caused by genetic and/or nongenetic factors.

[20] R. Laxova, "Guidelines for Clinical Genetic Services for the Public's Health," in *Genetic Services: Developing Guidelines for the Public's Health*, proceedings of a conference held in Washington, D.C., February 16–17, 1996, 9, 10. Affected births include chromosomal disorders (e.g., Down syndrome) single-gene disorders (e.g., sickle cell disease), disorders caused by identified environmental exposures (e.g., exposure to drugs such as thalidomide or accutane), and congenital disorders or malformations of multifactorial and/or unknown etiology.

[21] See M. J. Khoury and the Genetics Working Group, "From Genes to Public Health: The Applications of Genetic Technology in Disease Prevention," *American Journal of Public Health* 86 (1996): 1717, 1718–1719.

[22] L. D. Botto et al., "Neural Tube Defects," *New England Journal of Medicine* 341 (1999): 1509.

[23] For a discussion of newborn screening, see Chapter 6.

[24] See Chapter 6.

prenatal and pediatric populations. Some state health agencies also regulate genetic testing laboratories and clinical care centers and license medical professionals.[25]

### *Federal Activities*

The Maternal and Child Health Bureau (MCHB) of the Health Resources and Services Administration (HRSA), dedicated to advancing the health of "our nation's mothers, infants, children, and adolescents," has provided funding and leadership to states for development of genetic services since the 1950s.[26] The program supported establishment of child development clinics, state newborn screening programs, and cytogenetic laboratory training programs. In 1978, the National Genetic Disease Act created the Genetics Service Branch of MCHB to facilitate the early identification of individuals with genetic conditions and assist them in accessing appropriate systems of care.[27] In 1985, the federal government also funded the Council of Regional Networks for Genetics Services (CORN), a national organization that linked ten regional genetic services provider networks.[28] Federal agencies also play a lead role in quality assurance issues for genetic testing in clinical laboratories.[29]

## New Directions in Public Health Genetics

With overall morbidity and mortality caused by infectious disease in developed countries declining, and with the health implications of the new knowledge generated by the Human Genome Project, public health genetics services are expanding to encompass the more common complex disorders of childhood (e.g., asthma) and adulthood (e.g., cancer and cardiovascular disease) that result from the interplay of multiple genetic and environmental factors.[30]

In 1996, in response to developments in genetics research and to the Institute of Medicine's directive for public health to focus preventive activities for chronic adult diseases,[31] Dr. David Satcher, then the Director of the Centers for Disease Control and Prevention (CDC), established an agency-wide Task Force on Genetics and Disease

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[25] Other state agencies may oversee these and related functions. For example, in New York State, the Education Department oversees licensure of medical professionals. See the New York State Education Department website: *http://www.nysed.gov*, visited May 24, 2000.

[26] Maternal and Child Health Bureau website: *http://www.mchb.hrsa/gov/html/historymission.html*, visited May 11, 2000. The program was authorized in Title V of the Social Security Act of 1935.

[27] The National Genetic Disease Act (Title XI of the Public Health Service Act) was passed by Congress in 1976 and implemented in 1978. Maternal and Child Health Bureau website: *http://www.mchb.hrsa/gov/htm/genetics.html*, visited May 24, 2000.

[28] Council of Regional Networks for Genetic Services website: *http://www.cc.emory.edu/PEDIATRICS/corn/office/mission.htm*, visited May 22, 1998.

[29] See pages 319–321 and 328–332, this chapter.

[30] See Bloom, "The Future of Public Health," C63; see also *Genetics and Public Health in the 21st Century*, ed. M. J. Khoury, W. Burke, and E. J. Thompson (New York: Oxford University Press, 2000).

[31] See page 310, this chapter.

Prevention.[32] In 1997, the Task Force issued a strategic plan for strengthening and coordinating public health genetics activities, and the agency established a CDC Office of Genetics and Disease Prevention.[33] This office, alongside other federal and state health agencies, seeks to carry out the strategic plan through oversight, research, surveillance, education, and policy activities.Public Health and Genetics: Assessment Activities

### Population Surveillance

Public health surveillance refers to monitoring distributions and trends of morbidity and mortality data.[34] Surveillance can identify emerging epidemics and sometimes point the way to research and interventions, for example, by indicating an environmental source of communicable disease such as contaminated water sources. Chronic disease registries, such as the New York State Department of Health Cancer Registry, provide information about

population disease incidence and can highlight needs for targeted public health intervention (e.g., the need for breast cancer screening to promote earlier diagnosis).[35]

Genetic public health surveillance has generally focused on distributions and trends of single-gene disorders and birth defects.[36] For example, birth defect surveillance systems obtain baseline information to monitor changes in the prevalence of specific types of birth defects in specific locations.[37] Many states also monitor the occurrence of spontaneous abortions, congenital malformations, and perinatal morbidity.[38]

## Molecular Genetic Epidemiology Research

In addition to collection of population morbidity statistics, public health agencies can promote the health of populations by research to determine both the genetic and environmental components of disease and disability. Epidemiology, "the study of the distribution and determinants of health-related states or events in populations, and the application of this study to

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[32] Centers for Disease Control and Prevention, *Translating Advances in Human Genetics into Public Health Action* (Atlanta: Centers for Disease Control and Prevention, 1997), 2.

[33] Ibid., see Centers for Disease Control and Prevention Office of Genetics and Disease Prevention website: *http://www.cdc.gov/genetics*, visited January 10, 2000. For further discussion, see page 336, this chapter.

[34] A. D. Langmuir, "The Surveillance of Communicable Diseases of National Importance," *New England Journal of Medicine* 268 (1963): 182; see also A. Morabia, "Annotation: From Disease Surveillance to the Surveillance of Risk Factors," *American Journal of Public Health* 86 (1996): 625.

[35] See New York State Department of Health website: *http://www.health.state.ny.us/nysdoh/chronic/canreg.htm*, visited May 24, 2000.

[36] Birth defects are any morphological abnormality present at birth; they may have a genetic basis or they may be environmentally induced (or both). R. C. King and W. C. Stansfield, *A Dictionary of Genetics*, 5th ed. (New York: Oxford University Press, 1997), 41.

[37] Laxova, "Guidelines for Clinical Genetic Services for the Public's Health," 11.

[38] F. Desposito and C. Reid, "Clinical Genetic Services and Their Relevance to Public Health," in *Genetic Services: Developing Guidelines for the Public's Health*, proceedings of a conference held in Washington, D.C., February 16–17, 1996, 67, 68. For information about the New York State Department of Health Congenital Malformation Registry, see New York State Department of Health website: *http://www.health.state.ny.us/nysdoh/cmr.cmrback.htm*, visited August 4, 2000.

control health problems," is viewed as the scientific core of public health.[39] Genetic epidemiology research studies the role of genetic factors in diseases within a population.[40] It can identify population-specific gene variants that result in single-gene disorders such as phenylketonuria and beta-thalassemia.[41] It also can identify susceptibility variants for congenital birth defects such as cleft palate,[42] chronic adult diseases such as cancer, and infectious diseases, including HIV infection.[43]

A new genre of epidemiological research, molecular genetic epidemiology, studies how disease occurrence is linked to specific genetic variants, or biomarkers,[44] which may influence sensitivity to specific environmental agents.[45] Such studies provide a potential leap forward in the ability to identify both the genetic and environmental components of complex diseases, which generally evolve over a period of years, often decades. For example, the Framingham Heart Study, which began in 1948 and links long-term disease outcomes to personal behaviors and environmental factors, has added the use of molecular genetic population markers as a new dimension to its data analysis.[46] In another study, researchers examined how population variations of a single DNA base, called single nucleotide polymorphisms, or SNPs (pronounced "snips"),[47] may be associated with hypertension.[48]

Such research is part of a shift in epidemiologic surveillance and research from statistical associations to a greater emphasis on biological mechanisms of disease.[49] This research may eventually provide useful information about who in the population, based on inherited gene variants, might be candidates for predictive tests and preventive interventions. For example, study of one particular genetic population variant can identify persons at higher than average risk

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[39] M. J. Khoury, "Human Genome Epidemiology: Translating Advances in Human Genetics into Population-Based Data for Medicine and Public Health," *Genetics in Medicine* 1 (1999): 71, 72, quoting from J. M. Last, "A Dictionary of Epidemiology," 2d ed. (New York: Oxford University Press, 1995).

[40] Khoury, "Human Genome Epidemiology," 72.

[41] See A. DiRienzo, "Studies of Populations and Genetic Diseases: Mixing It Up," *Trends in Genetics* 14 (1998): 218; L. L. McCabe and E. R. B. McCabe, "Population Studies of Allele Frequencies in Single Gene Disorders: Methodological and Policy Considerations,"*Epidemiological Reviews* 19 (1997): 52.

[42] M. J. Khoury, T. H. Beaty, and S.-J. Hwang, "Detection of Genotype-Environment Interaction in Case-Control Studies of Birth Defects: How Big a Sample Size?" *Teratology* 51 (1995): 336.

[43] M. Carrington et al., "Genetics of HIV-1 Infection: Chemokine Receptor CCR5 Polymorphism and Its Consequences," *Human Molecular Genetics* 8 (1999): 1939; M. Roger, "Influence of Host Genes on HIV-1 Disease Progression," *FASEB Journal* 12 (1998): 625.

[44] For a discussion of genetic biomarkers, see Chapter 3, page 73.

[45] Khoury, "Human Genome Epidemiology," 72.

[46] R. Voelker, "Two Generations of Data Aid Framingham's Focus on Genes," *Journal of the American Medical Association* 279 (1998): 1245. In 2000, Boston University, which administers the study, announced formation of a company, Framingham Genomic Medicine, to use these data for pharmaceutical development. See G. Kolata, "Boston U. Founds a Company to Sift Landmark Heart Data," *New York Times*, June 17, 2000, A9.

[47] For a discussion of SNPs, see Chapter 1, page 25.

[48] See M. K. Halushka et al., "Patterns of Single-Nucleotide Polymorphisms in Candidate Genes for Blood-Pressure Homeostasis," *Nature Genetics* 22 (1999): 239.

[49] G. S. Omenn, "Comment: Genetics and Public Health," *American Journal of Public Health* 86 (1996): 1701, 1702.

for cardiovascular impairments whose risk can be reduced by increasing circulating levels of folic acid.[50]

### *Federally Sponsored Research*

Molecular epidemiological research to guide both public health and medical policy requires collaboration among private and public partners, including clinical geneticists, research scientists, public health practitioners, and consumer organizations.[51] The CDC Office of Genetics and Disease Prevention has a key role in sponsoring research and promoting essential collaborations and data dissemination.[52] It funds some external research projects and sponsors conferences and workshops (for example, a 1999 workshop on the genetics of congenital hearing impairment).[53] It also launched the Human Genome Epidemiology Network (HuGE Net) to promote international collaboration in the development and dissemination of molecular genetic epidemiologic data and information via the World Wide Web.[54]

### *New York State Research Activities*

At the Wadsworth Center of the New York State Department of Health, the Laboratory of Clinical Genetics and Genetic Epidemiology, created in 1969, acts as a diagnostic resource "for the purposes of initiating and conducting investigations of the causes, mortality, methods of treatment, prevention and cure of birth defects and genetic and allied diseases."[55] The laboratory currently performs cytogenetic (chromosome) analysis for congenitally affected infants, neonatal deaths, stillbirths, and spontaneous abortions.

In 1997, the department established the Laboratory of Molecular Genetic Epidemiology.[56] This laboratory complements the newborn screening program[57] by providing additional DNA-based testing for specific cases in which newborn bloodspots require follow-up testing to confirm or rule out a diagnosis. The laboratory also uses anonymized residual newborn bloodspots to analyze population frequencies of particular gene variants (alleles) to assess how their inheritance may influence risk for common complex disorders such as

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[50] See ibid., 1702.
[51] Khoury, "Human Genome Epidemiology," 72; The Human Genome Epidemiology Network (HuGE Net) website: *http://www.cdc.gov/genetics/ hugenet*, visited May 10, 2000.
[52] Ibid.; see also the Centers for Disease Control and Prevention Office of Genetics and Disease Prevention website: *http://www.cdc.goc/genetics*, visited May 10, 2000.
[53] Centers for Disease Control and Prevention and Gallaudet University, *Proceedings of the Workshop on the Genetics of Congenital Hearing Impairment* (Chamblee, Georgia, June 7, 1999), Centers for Disease Control and Prevention website: *http://www.cdc.gov/nceh/programs/CDDH/ddgen.htm*, visited September 30, 1999.
[54] Khoury, "Human Genome Epidemiology," 72–73.
[55] N.Y. Pub. Health Law § 2730 (McKinney 2000). See New York State Department of Health website: *http://www.wadsworth.org/testing/molecgen.htm*, visited April 4, 2000.
[56] Ibid.
[57] For a discussion of New York State Department of Health's Newborn Screening Program, see Chapter 6, page 149.

cardiovascular disease and cancer.[58] The Wadsworth Center also conducts basic genetics research to uncover fundamental knowledge about how genes work in health and disease.[59]

## Public Health and Genetics: Policy Activities

The Institute of Medicine Committee for the Study of the Future of Public Health recommended that public health agencies "serve the public interest in the development of comprehensive public health policies by promoting use of the scientific knowledge base in decision making about public health and by leading in developing public health policy."[60] To accomplish this requires a strategic approach that is respectful of the democratic process. At the federal and state levels, ongoing policy activities aim to translate scientific and medical discoveries about genetics into guidelines, regulations, and legislation to promote the public's health. Many examples are addressed in this report, including federal and state legislative initiatives to prevent the use of genetic information in insurance underwriting,[61] state efforts to ensure confidentiality of genetic information,[62] and state consideration of licensure or certification of genetic counselors.[63]

## Public Health Role in Genetic Screening

One area in which public health officials continue to face issues of translating genetics science to clinical practice is in the area of genetic screening. In the 1960s, premature implementation of mandatory state newborn screening for phenylketonuria (PKU) caused harm to some infants.[64] In the 1970s, misguided enthusiasm and poor science led to national promotion of sickle cell screening programs and legislation that lacked defined goals, produced no real benefits, and seriously harmed some who were screened.[65] These results prompted national policy groups to develop guiding principles to aid public and private partners in consideration and implementation of future population screening activities. These policy recommendations, combined with medical and scientific progress, have resulted in safe and effective newborn screening for PKU,

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[58] For a discussion on the retention, anonymization, and research use of residual newborn bloodspots, see Chapter 6, page 157. Although sample anonymization removes all identifying information that would allow the sample to be linked to its source, for large enough sample groups it may be possible to retain certain demographic information (e.g., race/ethnicity, county of origin) that is useful to epidemiologic research.

[59] See New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/divisions/gendis.htm*, visited May 24, 2000.

[60] Institute of Medicine Committee for the Study of the Future of Public Health, *The Future of Public Health*, 8.

[61] See Chapter 10.

[62] See Chapter 9.

[63] See Chapter 12, pages 357–361.

[64] For a discussion, see Chapter 6, page 143.

[65] For a discussion, see Chapter 5, page 114.

sickle cell disease, and other disorders[66] and reproductive carrier screening for sickle cell disease that is a standard of care.[67]

Several years ago, some proposed implementation of a new DNA-based genetic screening test to detect adults at risk for the iron storage disorder hemochromatosis. In response, the CDC and the National Human Genome Research Institute (NHGRI) sponsored a meeting to evaluate the scientific evidence and to consider related issues.[68] The panel concluded unanimously that it would be premature to implement population-based DNA screening, citing two factors: (1) limitations of the test's predictive power at that time[69] and (2) concerns regarding possible stigmatization and discrimination against those who test positive. Following this report, the National Heart, Lung, and Blood Institute launched a five-year, multiethnic, multicenter study to develop the data necessary to judge the feasibility, benefits, and risks of screening.[70]

### Addressing the Ethical, Legal, and Social Implications of the Human Genome Project

When the Human Genome Project activities of the NHGRI and the U.S. Department of Energy (DOE) commenced in 1990, each institution created an office to address the particular ethical, legal, and social concerns arising from the project.[71] Known as the Ethical, Legal, and Social Implications (ELSI) Programs, they direct 3 to 5 percent of their Human Genome Project research budgets to address concerns about social harms associated with the rapid translation of genetic science into clinical practice.[72] These separate but complementary programs have funded extramural research and education projects in four program areas: (1) privacy and fair use of genetic information, (2) clinical integration of genetic science, (3) genetic research, and (4) genetics education and resources.[73]

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[66] See Chapter 6, pages 143–144.

[67] See Chapter 5, page 116.

[68] W. Burke et al., "Hereditary Hemochromatosis: Gene Discovery and Its Implications for Population-Based Screening," *Journal of the American Medical Association* 280 (1998): 172, 175–177.

[69] Ibid., see also M. E. Cogswell et al., "Iron Overload, Public Health, and Genetics: Evaluating the Evidence for Hemochromatosis Screening," *Annals of Internal Medicine* 129 (1998): 971; A. S. Tavill et al., "Clinical Implications of the Hemochromatosis Gene," *New England Journal of Medicine* 341 (1999): 755. These limitations are the two general limitations of DNA-based tests, genetic heterogeneity and incomplete penetrance. See Chapter 2, page 41.

[70] National Heart, Lung, and Blood Institute website: *http://nhbli.nih.gov/nhbli/rafs/rfp9903.htm*, visited February 1, 1999.

[71] For a discussion, see Chapter 4.

[72] The NHGRI directs 5 percent of its budget to its ELSI Program; the U.S. DOE Human Genome Project directs 3 percent of its budget. See ELSI Research Planning and Evaluation Group, *A Review and Analysis of the Ethical, Legal and Social Implications (ELSI) Research Programs at the National Institutes of Health and the Department of Energy* (Washington, D.C.), February 10, 2000.

[73] ELSI Research Planning and Evaluation Group, *A Review and Analysis of the Ethical, Legal and Social Implications (ELSI) Research Programs*, 2. The New York State Task Force on Life and the Law's deliberations on genetic testing and screening were supported in large part by a grant from the NHGRI ELSI Program.

In addition, the ELSI Programs have sponsored working groups to address issues of major concern. For example, the 1997 NIH-DOE Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing (NIH-DOE Task Force on Genetic Testing) addressed concerns surrounding inadequate oversight of laboratory genetic testing.[74] The NHGRI ELSI Program also established an Office of Policy and Public Affairs to develop and disseminate information about genetics policy and legislative issues and to sponsor conferences and workshops in this area.[75]

## Public Health and Genetics: Assurance Activities

### Oversight: Assurance of Safe and Effective Genetic Testing

The purpose of regulatory oversight of clinical laboratories is to ensure that laboratory testing provides clinically meaningful information and that laboratories performing the tests provide accurate and reliable results. One essential measure is analytical validity — how well a test, and the laboratory performing the test, measures the property or characteristic it is intended to measure, for example, whether a particular gene mutation is present.[76] Another critical measure is clinical validity, the ability of a positive test result to detect current disease or predict future disease (positive predictive value) and of a negative test result to rule out current or future disease (negative predictive value).[77] A third parameter, clinical utility, is a measure of whether, and to what extent, a test result provides clinically useful information to the person tested and their doctor.[78] For example, some tests, such as the DNA-based test to detect familial mutations for Huntington disease, have high clinical validity, that is, this test can definitively determine whether an individual will develop Huntington disease later in life — but its clinical utility is questionable, given that there are no preventive measures available for individuals who test positive.[79]

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[74] National Institutes of Health-Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing in the United States*, ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of Health, 1997). For further discussion, see page 329, this chapter.

[75] See National Institute of Human Genome Research website: *http://www.nhgri.nih.gov/ELSI*, visited May 22, 2000.

[76] For further discussion, see Chapter 2, page 41. Secretary's Advisory Committee on Genetic Testing, *Adequacy of Oversight of Genetic Tests: Preliminary Conclusions and Recommendations of the Secretary's Advisory Committee on Genetic Testing*, April 12, 2000, 13–14. The report is available at the National Institutes of Health website: *http://www4.od.nih.gov/oba/ sacgt.htm*, visited April 25, 2000.

[77] For a discussion, see Chapter 2, page 42.

[78] For a discussion, see Chapter 2, page 43.

[79] Some groups use the term clinical utility more broadly, to include any utility based on knowledge of the test information, even if no clinically useful interventions are available. See, e.g., Secretary's Advisory Committee on Genetic Testing, *Adequacy of Oversight of Genetic Tests*, 13. In this context, predictive testing for Huntington disease can provide useful information to guide individuals in reproductive and other choices. See Chapter 3, page 61.

### *Federal Oversight of Genetic Testing*

*New Test Approval*

All clinical laboratory tests, including genetic tests, may be marketed either as kits or services. Tests marketed as kits include pre-assembled components necessary to perform a test along with instructions on how to use them. Kits are sent to other laboratories, physician offices, or even to consumers who may perform the test themselves. By contrast, tests marketed as services are performed by reference laboratories that receive specimens for in-house testing. The testing laboratory receives the sample from a referring physician, along with pertinent clinical information about the patient, and reports back to the physician.[80]

The Food and Drug Administration (FDA) is responsible for approval of laboratory tests marketed as kits under the Federal Food, Drug, and Cosmetics Act,[81] which requires that these tests have both analytical validity and clinical validity.[82] The FDA does not assess a test's clinical utility. Currently in the United States, genetic tests are not offered as kits. However, rapid changes in test technologies, including DNA chip technology, make it possible that future genetic tests may be prepackaged as kits for purchase and performance by physicians in their own offices.[83]

Currently, most genetic tests are provided as services, usually at the request of a physician. Although the FDA has legal authority to review and approve tests provided as services, up until recently it has not exercised that authority. It also has chosen not to require organizations developing such tests under investigational protocols to obtain approval by an institutional review board (IRB).[84] Since 1998, however, the FDA has regulated oversight of "home brew" reagents. These are the active ingredients prepared by manufacturers for sale and use in tests provided as services by individual laboratories (e.g., antibodies and nucleic acid sequences).[85]

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[80] See J. Amos and B. Gold, "Testing Environment for Single-Gene Disorders in U.S. Reference Laboratories," *Human Mutation* 12 (1998): 293.

[81] 42 U.S.C.A. § 263a et seq. (West 2000).

[82] This requirement is designated by the Medical Device Amendments to the Food, Drug, and Cosmetic Act, which requires premarket demonstration of clinical testing devices, including genetic testing devices. See NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 29–30. 21 U.S.C.A. § 360e (West 2000).

[83] N. A. Holtzman, "Promoting Safe and Effective Genetic Tests in the United States: Work of the Task Force on Genetic Testing," *Clinical Chemistry* 45 (1999): 732, 738; Dr. Anthony Carrano, Director, Biology and Biotechnology Research Program, Lawrence Livermore National Laboratories, "Technological Advances in Genomic Analysis," presentation at *Implications of Individualizing Medicine through Genomics*, Stanford University, October 1998.

[84] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 30.

[85] "Medical Devices: Classification/Reclassification; Restricted Devices; Analyte Specific Reagents," *Federal Register* 62 (1997): 62243. See also S. Gutman, "The Role of Food and Drug Administration Regulation of In Vitro Diagnostic Devices — Applications to Genetic Testing," *Clinical Chemistry* 45 (1999): 746, 748–749. This regulation, which became effective November 23, 1998, subjects manufacturers of analyte-specific reagents to basic controls including good manufacturing processes.

*Laboratory Quality Assurance*

Once laboratory tests are offered by a laboratory for patient-identified testing, they are subject to oversight under the federal Clinical Laboratory Improvement Amendments of 1988 (CLIA).[86] The Health Care Financing Administration (HCFA), under CLIA, certifies laboratories that provide tests as services. However, HCFA monitors a test's analytical validity only — it does not monitor clinical validity or clinical utility.[87] The program requires laboratory inspections every two years. Such surveys monitor laboratory operating environment, personnel, quality control and quality assurance, and proficiency testing.[88] CLIA assigns a complexity level to each test according to established criteria. Tests of high complexity are subject to more stringent personnel and quality control requirements.[89]

CLIA recognizes distinct categories of laboratory practice (e.g., microbiology and hematology) but does not recognize genetic testing as a separate category, presumably because genetics was not yet recognized as a specialty area when the test categories were established.[90] In one survey, only 39 percent of nonprofit organizations and 53 percent of biotechnology companies that were considered likely to be developing or providing new genetic test technologies agreed that current CLIA requirements were adequate to "assure the quality of genetic test services."[91] All genetic testing is categorized as high complexity testing unless specifically categorized otherwise.

*New York State Oversight*

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[86] 42 U.S.C.A. 263 et seq. (West 2000); 57 Fed. Reg. 7002 (1992). The 1988 modification of CLIA was perceived as a "sea change" in the regulation of clinical laboratories. It requires labs to comply with prescriptive norms concerning personnel standards, patient test management, quality control assurance, and proficiency testing. Stringency varies with level of test complexity. See M. K. Schwartz, "Genetic Testing and the Clinical Laboratory Improvement Amendments of 1988: Present and Future," *Clinical Chemistry* 45 (1999): 739.

[87] HCFA is the federal agency with primary responsibility for the administration of CLIA.

[88] For proficiency testing, a laboratory is supplied with test specimens. The supplier, but not the laboratory, knows the composition (e.g., presence of a mutation or quantitative level of an enzyme). Laboratories are expected to analyze the test sample as they would a patient specimen and provide results to the supplier. NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 48.

[89] Ibid., xvii–xviii.

[90] Schwartz, "Genetic Testing and the Clinical Laboratory Improvement Amendments of 1988," 739.

[91] N. A. Holtzman and S. Hilgartner, "State of the Art of Genetic Testing in the United States: Survey of Biotechnology Companies and Nonprofit Clinical Laboratories and Interviews of Selected Organizations," in NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 104.

Some state health agencies license clinical laboratories and laboratory personnel.[92] New York State has the most far-reaching requirements for both test approval and laboratory oversight.[93] It requires all clinical laboratories located in New York, or located outside New York but accepting diagnostic specimens originating in New York, to obtain a permit in order to perform testing as a service.[94] The Wadsworth Center, which is part of New York State Department of Health, oversees laboratories that perform tests provided as services and makes all permitting decisions through the Laboratory Reference System.[95] This program oversees the verification of performance of such assays as offered by permit laboratories. It does not oversee manufacturers' tests that are provided as kits.

For licensure purposes, the Laboratory Reference System defines genetic testing as "procedures performed for the purpose of providing information for the diagnosis of a genetic disease or its carrier state," using DNA-based methodologies and/or biochemical techniques.[96] Cytogenetic analysis of chromosomes and maternal serum alpha-fetoprotein testing are regulated under other categories. The program does not consider clinical genetic testing to be different from other forms of clinical laboratory testing.[97]

*Laboratory Quality Assurance*

New York's Laboratory Reference System requires that clinical testing laboratories demonstrate the reliability of their testing methods and laboratory personnel standards.[98] Permitted laboratories are subject to on-site inspections and must engage in some form of proficiency testing.[99] Testing laboratories within New York State are exempt from federal CLIA oversight because of the New York program's stringent criteria.[100] Several other states have less stringent licensure requirements for laboratories providing genetic tests.

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[92] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 118–121. The report cites ten states with genetic testing licensure requirements.

[93] Ibid.; NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 41.

[94] N.Y. Pub. Health Law § 574 (McKinney 2000). Violation of this requirement may result in civil and/or criminal penalties against the laboratory's director and owner. Ibid., §§ 12-b(2), 577.

[95] Requirements for licensure are applicable to all clinical laboratories except those operated solely as an adjunct to the treatment of a physician's patients or operated by the federal government. See New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/labcert/clep/clep.html*, visited February 23, 1999.

[96] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, "Genetic Testing Quality Assurance Program of the New York State Clinical Laboratory Evaluation Program," unpublished memorandum provided during a presentation to the New York State Task Force on Life and the Law, February 20, 1998. The definition excludes testing for acquired, nonheritable mutations or for infectious agents and testing for identification purposes.

[97] Ibid.

[98] See New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/labcert/cleoinfo/clep.html*, visited February 9, 2000.

[99] For discussion of proficiency testing, see page 320, this chapter.

[100] New York State Department of Health Wadsworth Center website: *http://www.wadsworth.org/labcert/cleoinfo/clep.html*.

*Reviewing Tests for Analytical and Clinical Validity*

New York's Laboratory Reference System requires review and approval of all new clinical laboratory tests that are performed as services in permitted laboratories. Tests are reviewed based on demonstrated analytical validity and purported clinical validity where data are available. The program's oversight program is the only government entity in the country that assesses the clinical validity of genetic tests. In 1997, a national panel that was established to review and make recommendations about federal oversight of genetic testing cited New York State's leadership in this area as the basis for its own recommendation that all genetic tests have demonstrated clinical validity.[101] New York's program does not consider a test's clinical utility; it perceives this judgment to be in the purview of the physician and the patient.[102] In its review, the New York program also examines educational brochures, informed consent forms, and a model test result form, although it has no legal authority to require specific content or conduct of the consent process.[103]

Until 1999, the New York program's approval decisions were made by the pertinent section head of the testing category, for example, genetic testing. In 1999, the program proposed initiation of a Clinical Testing Review Panel (CTRP) to consider new tests requiring clinical validation review.[104] The CTRP will be chaired by a research physician experienced in laboratory medicine. The program's director (or designee), the pertinent section head (or designee), and one additional reviewer expert in the area of clinical application of the test shall serve on the panel as convened for review of each assay.[105] Unanimous decisions are to be final; absent unanimity, decisions are to be made by the department's Wadsworth Center Director.

Approval of new tests is generally a four- to six-month process, but laboratory permit applicants may request expedited review, generally requiring six to eight weeks from the

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[101] Dr. Neil Holtzman, Chairman of the NIH-DOE Task Force on Genetic Testing, presentation to the New York State Task Force on Life and the Law, February 20, 1998.

[102] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, presentation to the New York State Task Force on Life and the Law, February 20, 1998.

[103] Ibid.

[104] Telephone conversation with Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, February 2, 2000; New York State Department of Health Wadsworth Center Laboratory Reference System, *Procedures for Addition of New Clinical Laboratory Assays by New York State Permitted Laboratories*, draft document, March 1999.

[105] Laboratory Reference System, *Procedures for Addition of New Clinical Laboratory Assays by New York State Permitted Laboratories*.

time of application.[106] In 1999, the program began review of its approval process and has attempted to attain a thirty-day review period for new tests.[107]

The program also has a procedure by which physicians may request that testing be performed by an unpermitted laboratory if a test is not provided by a permitted laboratory. This allowance, for which there is no explicit legal authorization,[108] is intended to facilitate testing for rare genetic disorders (incidence of less than 1/100,000) or for other cases in which a required test is not provided by a laboratory holding a valid New York State clinical laboratory permit.[109]

*Categorization of Test Approval*

The New York Laboratory Reference System recognizes categories, or levels, of test approval for all clinical laboratory tests, including genetic tests.[110] Generally accepted tests include tests that are FDA approved or are determined to be clinically valuable "by physicians or other authorized persons, or by consensus groups convened by a nationally recognized association, society, or expert in the specialty."[111] One example is genetic testing for hemoglobinopathies such as sickle cell disease. Other tests may be approved as investigational tests. Investigational tests do not meet the above criteria but have been determined "by the department to be of potential clinical value and reliability based on data developed from research use of the test."[112]

For such investigational tests, additional requirements include written informed consent from both the physician and the patient,[113] collection of clinical validation data for those tested, and, "whenever required by Article 24-A of the Public Health Law, approval

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[106] Ibid. Telephone conversation with Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, February 2, 2000. The time periods are from the time of submission of all application materials and information required for review.

[107] Dr. Lawrence Sturman, Director, Wadsworth Center, New York State Department of Health, presentation to the New York State Task Force on Life and the Law, March 29, 1999; Laboratory Reference System, *Procedures for Addition of New Clinical Laboratory Assays by New York State Permitted Laboratories*.

[108] See N.Y. Pub. Health Law § 574 (McKinney 2000) (requiring laboratories that perform clinical testing to have permits from the New York State Department of Health).

[109] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, "Genetic Testing Quality Assurance Program of the New York State Clinical Laboratory Evaluation Program."

[110] The program does not oversee testing for research purposes in which test results are not provided to the person from whom the blood or other tissue is obtained.

[111] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, "Genetic Testing Quality Assurance Program of the New York State Clinical Laboratory Evaluation Program."

[112] A. M. Willey, "Genetic Laboratory Medicine in the 21st Century: New Tests, New Regulations?" *The Genetic Resource* 6, no. 2 (1992): 25, 26.

[113] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, "Genetic Testing Quality Assurance Program of the New York State Clinical Laboratory Evaluation Program." This requirement is prior to and independent of New York State genetic testing legislation (N.Y. Civ. Rights Law § 79-l (2)(b) (McKinney 1999)) that requires informed consent for all genetic testing.

from the research facility's IRB for protection of human subjects."[114] Designation of a test as investigational also has implications for third-party payer reimbursement, including Medicaid and Medicare, as payers are less likely to cover costs of tests that are not generally accepted.[115] Examples of genetic tests that are approved by New York State as investigational are BRCA1 and BRCA2 testing for breast cancer susceptibility and carrier, prenatal, or diagnostic testing for Fragile X, a disorder associated with mental retardation.

The Laboratory Reference System is considering an approval process in which tests are approved in a single category with specific limitations or restrictions as necessary.[116] This approach could mitigate concerns about exclusion of investigational test costs by third-party payers. It also could provide relevant test-specific information to guide ordering decisions by physicians and payer reimbursement decisions.

*Permitted Laboratories and Permit Fees*

As of February 2000, New York's Laboratory Reference System permitted genetic testing for about fifty-five disorders.[117] It had active permits for almost seventy laboratories that perform DNA-based and/or biochemical genetic tests, thirty-eight of which are located outside New York State. The program issues permits to an additional fifty-five cytogenetic testing laboratories.

Laboratories must obtain approval for each test they wish to offer for specimens originating in New York State.[118] Most large out-of-state commercial genetic testing laboratories, which perform 25 to 50 percent of genetic testing in the United States, hold New York State permits. However, many of these laboratories hold New York permits for only a subset, sometimes a minority, of all genetic tests they offer.[119]

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[114] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, "Genetic Testing Quality Assurance Program of the New York State Clinical Laboratory Evaluation Program."

[115] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, presentation to the New York State Task Force on Life and the Law, February 20, 1998. For a discussion of federal entitlement program coverage policies see M. J. Mehlman, "Access to the Genome and Federal Entitlement Programs," in *The Human Genome Project and the Future of Health Care*, ed. T. H. Murray, M. A. Rothstein, and R. F. Murray (Indianapolis: Indiana University Press, 1996), 113.

[116] Telephone interview with Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, February 2, 2000.

[117] Dr. Ann Willey et al., Wadsworth Center, New York State Department of Health, in a letter of public comment from the New York State Department of Health Wadsworth Center as part of public comment to the Secretary's Advisory Committee on Genetic Testing, February 14, 2000.

[118] Ibid. This is required under N.Y. Pub. Health Law § 570 (McKinney 2000).

[119] Ibid. For example, in March 1999, one commercial laboratory, Athena Diagnostics, Inc., was permitted by New York State to perform eight of the thirty-nine genetic tests listed as clinically available by Athena Diagnostics on Helix (now known as GeneTests™), a clinical genetic testing laboratory database sponsored by the National Library of Medicine. Baylor College of Medicine DNA Diagnostic Laboratory held New

All laboratories, regardless of the number of tests for which they seek approval, pay an initial application fee of $1,000 and an annual registration fee of $100.[120] Permitted laboratories also pay an annual laboratory inspection and reference fee that is based on the laboratory's gross annual receipts for clinical tests performed on specimens originating within New York State. The fees are calculated to recoup actual reference system operation costs.[121]

*Whom May Order Genetic Laboratory Tests*

In New York State, clinical laboratory tests, including genetic tests, may be ordered only by physicians and others authorized to do so.[122] This does not include Ph.D.s (with the exception of Ph.D. laboratory directors) or master's-level genetic counselors except when they function as the agent of a physician.[123] The Laboratory Reference System can provide physicians with a list of clinical genetics providers and encourages, but does not require their use for posttest analysis and counseling.[124] Laboratories must report test results to the physician who ordered the test and generally may not report results to the test subject directly.[125]

### *Concerns about Inadequate Oversight of Genetic Testing*

Some commentators, including several policy groups, have expressed concerns about oversight of predictive genetic testing. These commentators note the current limited degree of federal oversight, the rapid expansion of genetic technologies and clinical tests, the complexity of molecular genetic test performance and interpretation and associated errors, and the need for ongoing data collection to confirm clinical validity.[126] Some claim that special oversight is required for predictive genetic tests performed on healthy people because

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York State permits for three of its thirty-two listed clinically available genetic tests. See GeneTests™ website (formerly Helix): *http://www.helix.org*, visited March 2, 1999.

[120] Personal communication, Nanette Healy, Coordinator of Genetic Testing Quality Assurance Program, Wadsworth Center, New York State Department of Health, May 7, 1999. N.Y. Pub. Health Law § 575(4) (McKinney 2000). 10 N.Y.C.R.R. § 58-3.7 (2000).

[121] 10 N.Y.C.R.R. § 58-3.1(c), 58-3.2 (2000). Out-of-state laboratories also must pay travel expenses associated with laboratory inspections. 10 N.Y.C.R.R. § 58-3.8 (2000).

[122] 10 N.Y.C.R.R. § 58-1.7(b) (2000).

[123] Willey, "Genetic Laboratory Medicine in the 21st Century: New Tests, New Regulations?" 28.

[124] Dr. Ann Willey, Director, Office of Laboratory Policy and Planning, Wadsworth Center, New York State Department of Health, presentation to the New York State Task Force on Life and the Law, February 20, 1998.

[125] Ibid.; 10 N.Y.C.R.R. § 58-1.8 (2000). In one survey of national clinical genetic testing laboratories, 45 percent of laboratories surveyed responded that they occassionally had provided test results directly to consumers. D. C. Wertz and P. R. Reilly, "Laboratory Policies and Practices for the Genetic Testing of Children: A Survey of the Helix Network," *American Journal of Human Genetics* 61 (1997): 1163.

[126] See, e.g., Holtzman, "Are Genetic Tests Adequately Regulated?"; W. W. Grody and R. E. Pyeritz, "Report Card on Molecular Genetic Testing: Room for Improvement?" *Journal of the American Medical Association* 281 (1999): 845; R. A. Robinson, "Are We Failing in Molecular Genetic Testing?" *American Journal of Clinical Pathology* 112 (1999): 11; A. Paxton, "Fears Collide as Genetic Testing Moves Forward," *CAP Today* 13 (February 1999): 1.

of the special risks of psychological and discriminatory harm associated with the ability to determine probabilistic disease risk estimates many years ahead, often in the absence of useful clinical interventions.[127]

*Expanded Test Development*

GeneTests™, a national directory of laboratories performing disease-specific genetic testing, lists over 257 laboratories that perform clinical testing for 419 genetic disorders for which test results are reported back to the test subject;[128] the majority of these tests are DNA-based tests.[129] From 1994 to 1996, the number of genetic tests performed increased by at least 30 percent per year.[130] An advisory committee to the Secretary of Health and Human Services predicted that the Human Genome Project will continue to have a major impact on the development of new genetic tests.[131] Some have noted that this area of clinical testing is advancing more rapidly than other forms of clinical testing and is performed with limited federal oversight.[132]

*Evidence of Genetic Testing Errors*

One survey of genetic testing laboratories found that significant minorities of laboratories did not appropriately review tests before marketing and did not perform adequate proficiency testing.[133] Another survey found that a number of molecular genetic testing laboratories responding to a questionnaire showed scores that "may reflect suboptimal laboratory practices" for both laboratory personnel qualifications and laboratory practice standards.[134] Others, however, claim that limited evidence of harm to patients based on

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[127] Dr. Neil Holtzman, Chairman of the NIH-DOE Task Force on Genetic Testing, presentation to the New York State Task Force on Life and the Law, February 20, 1998. For a discussion about the risks of predictive genetic susceptibility testing, see Chapter 3, page 68.

[128] Generally, results are reported indirectly to the patient by a physician or other health care provider. GeneTests™ also has a category of research tests for which results are not reported to the test subject.

[129] GeneTests™, formerly known as Helix, website: *http://www.genetests.org*. The number of genetic disorders tested for is from a May 9, 2000, data summary report provided by GeneTests™. The term molecular genetic tests covers all DNA-based genetic testing. GeneTests™ separately lists laboratories that provide genetic tests for which test results are not provided to the test subject but are used for research purposes only.

[130] M. M. McGovern et al., "Quality Assurance in Molecular Genetic Testing Laboratories," *Journal of the American Medical Association* 281 (1999): 835. Based on data provided by GeneTests™, the number of disorders for which clinically genetic tests were available increased from 344 to 419 (22 percent) between September 1999 and May 2000.

[131] Secretary's Advisory Committee on Genetic Testing, *Adequacy of Oversight of Genetic Tests*, 2.

[132] Grody and Pyeritz, "Report Card on Molecular Genetic Testing," 845, 846.

[133] Holtzman and Hilgartner, "State of the Art of Genetic Testing in the United States," 99.

[134] McGovern et al., "Quality Assurance in Molecular Genetic Testing Laboratories," 835.

genetic testing errors indicates that such errors are rare and not more frequent than errors in other types of clinical testing.[135]

For predictive genetic tests, pretest and posttest phases are generally more complex than for other types of clinical testing,[136] and some have cited the high potential for misuse and misinterpretation of predictive genetic tests as a special concern.[137] For example, in one survey of errors by molecular genetic testing laboratories, the most common errors detected were in the pretest phase, including inappropriate test selection by the ordering physician.[138] A survey of 115 informational pamphlets provided by genetic testing laboratories to health care providers and/or patients found that genetic test information was "highly variable in content and potentially deficient or misleading."[139] Less than half of the pamphlets included statements about the accuracy of the test, and only one in five included information about test interpretation.[140] In another study, about one-third of physicians incorrectly interpreted a negative test result for a presymptomatic test to determine whether individuals were at risk for familial colon cancer.[141]

Many cases of testing errors and associated harms have been reported. In 1996, one clinical genetics specialist reported that over fifteen major lawsuits had been "initiated around the issues of negligence in Tay-Sachs testing."[142] In another case, a woman who was misinformed that she tested positive for a BRCA gene mutation and then underwent prophylactic surgery to remove her ovaries was later informed that the result was erroneous and she had not inherited the mutation.[143]

*Need for Ongoing Data Collection*

Increasingly, genetic tests are being developed not only for variants associated with single-gene disorders but also for susceptibility variants that confer increased risk for

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[135] W. T. Hofgartner and J. T. Tait, "Frequency of Problems during Clinical Molecular-Genetic Testing," *American Journal of Clinical Pathology* 112 (1999): 14, 17; see also Robinson, "Are We Failing in Molecular Genetic Testing?" 11; Grody and Pyeritz, "Report Card on Molecular Genetic Testing," 846.

[136] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, xx, 54–55.

[137] Ibid.; Robinson, "Are We Failing in Molecular Genetic Testing?" 11–12; V. Foubister, "Lapses in Practice, Oversight Undercut Genetic Testing," *American Medical News*, October 18, 1998, 8.

[138] Hofgartner and Tait, "Frequency of Problems during Clinical Molecular-Genetic Testing," 17.

[139] M. K. Cho, M. Arruda, and N. A. Holtzman, "Informational Materials about Genetic Tests," in *Promoting Safe and Effective Genetic Testing*, 125, 127.

[140] Ibid., 127.

[141] F. M. Giardiello et al., "The Use and Interpretation of Commercial APC Gene Testing for Familial Adenomatous Polyposis," *New England Journal of Medicine* 336 (1997): 823. In this case, a negative test result was not conclusive that a person was not at risk for cancer; only certain types of mutations are detectable by the method used.

[142] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 42 (quoting Michael M. Kabach, M.D., Director, International Tay-Sachs Disease Data Collection and Quality Control Program).

[143] R. Weiss, "Genetic Testing's Human Toll," *Washington Post*, July 21, 1999, A01. The testing laboratory was alerted to its error eight months after test performance when the test subject donated blood to a different laboratory performing BRCA gene research. The research laboratory was unable to detect the reported mutation.

complex late-onset diseases such as cancer and cardiovascular disease.[144] As of 1995, over fifty commercial companies were providing or developing predictive and diagnostic genetic tests; the single largest category was tests to detect risk for common complex diseases.[145]

For susceptibility tests to determine future disease risks in healthy adults, data collected for the original research studies that lead to development of the test often are not representative of findings in broader and different population groups, and confirmation of a test's clinical validity for such population groups may take years.[146] An added complication is that a single gene may have many, even hundreds, of different clinically relevant (or potentially relevant) mutations. Thus, clinical laboratory tests may be offered before clinical validity for some test results and/or for some populations is adequately established.[147]

For example, in the BRCA1 and BRCA2 breast and ovarian cancer susceptibility genes, over 1,000 mutations have been found, 35 percent of which are novel mutations unique to a particular person or family.[148] Reliable calculation of the predictive value of BRCA gene mutations in general, and specific calculations for certain mutations, requires years of follow-up studies to see how many women who test positive actually develop breast or ovarian cancer.[149] Myriad Genetic Laboratories, which holds the commercial rights to BRCA1 and BRCA2 gene testing, promotes the collection of such follow-up data and facilitates collaborative research with the National Institutes of Health.[150]

### *Recommendations for Improved Federal Oversight of Genetic Testing*

#### *The Institute of Medicine Committee on Assessing Genetic Risks*

In 1993, the Institute of Medicine's Committee on Assessing Genetic Risks expressed concerns about the lack of adequate federal oversight of genetic testing and stated that "the nature of genetic tests and their interpretation, and the magnitude of the personal and clinical decisions that may be based on such results," warrants "a standard with close to zero chance of error."[151]

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[144] For a discussion, see Chapter 3, page 62.
[145] Holtzman, "Are Genetic Tests Adequately Regulated?" 409.
[146] See Chapter 3, page 70; see also Chapter 5, page 126.
[147] Holtzman, "Are Genetic Tests Adequately Regulated?" 409; Paxton, "Fears Collide as Genetic Testing Moves Forward," 40.
[148] T. Reynolds, "NCI-Myriad Agreement Offers BRCA Testing at Reduced Cost," *Journal of the National Cancer Institute* 92 (2000): 596.
[149] See Chapter 3, page 64; see also Chapter 5, page 126. For some mutations, researchers can tell that the change to the DNA sequence will seriously impair or prevent normal production or functioning of the gene product (e.g., the BRCA1 protein). In some cases, however, researchers cannot determine whether or how a specific mutation might affect the function of the gene product.
[150] Reynolds, "NCI-Myriad Agreement Offers BRCA Testing at Reduced Cost," 596.
[151] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 11.

The NIH-DOE Task Force on Genetic Testing

In 1997, the National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing (NIH-DOE Task Force on Genetic Testing) found that federal oversight of the development and application of genetic tests is deficient and poses harms to the public health.[152] They expressed special concerns about predictive genetic tests performed in healthy or apparently healthy people.[153] They stated, "The Task Force strongly holds that the clinical use of a genetic test must be based on evidence that the gene being examined is associated with the disease in question, that the test itself has analytical and clinical validity, and that the test results be useful to the people being tested."[154] They also emphasized the importance of pretest and posttest phases of genetic testing — helping patients decide if they are appropriate candidates for testing and interpreting test results correctly.[155]

To address these problems, the NIH-DOE Task Force on Genetic Testing called for an active federal agency role (by the FDA or the CDC) in the approval of genetic tests that are performed as services.[156] It recommended that the Secretary of Health and Human Services establish a committee to consider agency responsibilities and practices.[157]

The NIH-DOE Task Force on Genetic Testing addressed the special concern of predictive genetic tests that may have some evidence of clinical validity but that require continued data collection to establish reliable levels of validity.[158] It expressed concern that "requirements for prolonged data collection might inhibit test development"[159] and made recommendations to promote the marketing of such tests and the collaboration of public and private organizations for continued data collection.[160] This "could allow

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[152] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*; see also N. A. Holtzman et al., "Predictive Genetic Testing: From Basic Research to Clinical Practice," *Science* 278 (1997): 602.

[153] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, xi.

[154] Ibid., 24.

[155] Ibid., xx, 54–55.

[156] See A. Huang, "FDA Regulation of Genetic Testing: Institutional Reluctance and Public Guardianship," *Food and Drug Law Journal* 53 (1998): 555. Huang states that this recommendation in the Task Force on Genetic Testing's report was "surprisingly murky" and suggests it may be because of a trend away from a central FDA role in oversight of genetic tests, in part because of the agency's reluctance to assume that role. Ibid., 555–556.

[157] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 10.

[158] The NIH-DOE Task Force on Genetic Testing recommended that after investigational data collection and before marketing, test developers should submit their validity and utility data for a structured internal (local) review, for independent external review, and for review by professional organizations, in order to permit informed decisions about routine use. Test review should include assessment of informational material provided about the test. Formal validation of each intended use of a genetic test (other than the original intended use) should be required before that use becomes generally accepted in clinical practice.

[159] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 35.

[160] Ibid., 35–36.

reimbursement, or coverage of, tests by third-party payers during investigative stages in which data are being collected."[161] It also recommended a requirement for local IRB approval of all such clinical genetic testing protocols and stated that the federal Office of Protection of Human Subjects from Research Risks should develop guidelines to assist the IRBs.[162]

The NIH-DOE Task Force on Genetic Testing also recommended that the CLIA program should establish a genetics specialty section and mandatory standardized national proficiency testing.[163] It recommended that predictive genetic tests should be designated as high complexity[164] and that testing laboratories present test results in a form that is understandable to the nongeneticist health care provider.[165]

*The Clinical Laboratory Improvement Advisory Committee Genetics Working Group*

In anticipation of the NIH-DOE Task Force on Genetic Testing's 1997 recommendations, the Clinical Laboratory Improvement Advisory Committee (CLIAC), established by CLIA in 1992 to advise the Secretary of Health and Human Services on scientific and technical matters, formed a genetics working group to review the need for changes in classification and oversight of genetic testing.[166] In 1998, CLIAC and its working group agreed that genetic testing is sufficiently different from other types of clinical laboratory testing to warrant recognition as a separate specialty section.[167] Their report includes specific recommendations for personnel, quality control, proficiency

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[161] Ibid., xvi.

[162] Ibid., xv, 33–34. The NIH-DOE Task Force on Genetic Testing recommended that test developers comply voluntarily with obtaining IRB approval.

[163] Ibid., 48–52. The NIH-DOE Task Force on Genetic Testing supported the intention of the CDC to create a genetics subcommittee to advise CLIA on the creation of a genetics specialty. Until CLIA establishes a genetic testing specialty, the Task Force called for laboratories performing DNA/RNA-based predictive tests to voluntarily participate in the College of American Pathologists' (CAP) molecular pathology program, including the CAP/American College of Medical Genetics (ACMG) proficiency testing program. The Task Force also recommended that CAP/ACMG periodically publish listings of laboratories performing genetic tests satisfactorily.

[164] Ibid., xvii–xviii, 44–45.

[165] Ibid., xx.

[166] Schwartz, "Genetic Testing and the Clinical Laboratory Improvement Amendments of 1988," 741; see also A. Paxton, "How Regulatory Agencies Are Addressing Genetic Testing," *CAP Today*, February 1999, 44.

[167] Clinical Laboratory Improvement Advisory Committee Summary Report (U.S. Department of Health and Human Services, January 29–30, 1998). See also Schwartz, "Genetic Testing and the Clinical Laboratory Improvement Amendments of 1988." In May 2000, the CDC, acting as scientific advisor to HCFA, issued a notice of proposed rule making to revise the CLIA regulations for human genetic testing based on CLIAC recommendations. Centers for Disease Control and Prevention, "Notice of Intent; Genetic Testing under the Clinical Laboratory Improvement Amendments," *Federal Register* 65 (May 4, 2000): 25928.

testing, validation of tests, and other facets of testing.[168] As a follow-up to these recommendations, a CDC-sponsored committee developed recommendations to improve quality assurance practices and proficiency testing programs for clinical laboratory molecular genetic testing for human heritable diseases.[169] In May 2000, the CDC announced its intent to revise CLIA regulations applicable to laboratories performing human genetic testing.[170]

*The Secretary's Advisory Committee on Genetic Testing*

The Secretary's Advisory Committee on Genetic Testing (the Secretary's Advisory Committee) was chartered in June 1998 and charged to advise the Secretary of Health and Human Services "about all aspects of the development and use of genetic tests, including the complex medical, legal, and social issues raised by genetic testing."[171] The U.S. Assistant Secretary of Health and Surgeon General, Dr. David Satcher, requested that the committee assess, with public consultation, the adequacy of oversight of genetic testing.[172]

In a preliminary report issued in April 2000, the Secretary's Advisory Committee agreed that additional oversight is warranted for all genetic tests.[173] It recommended that the FDA should be the lead agency for review, approval, and labeling of all new genetic tests.[174] It stated that FDA review should focus on claims of analytical and clinical validity made by the developer of the test. It also stated that the FDA should develop flexible review mechanisms and review tests in a manner "appropriate to the level of complexity of information generated by the test."[175]

The committee also stated that, in addition to analytical validity and clinical validity, other major criteria for assessing new genetic tests should include the test's clinical utility as well as "social considerations."[176] It stated that predictive tests require greater scrutiny than diagnostic tests and that susceptibility tests for low penetrance mutations (those less likely to contribute to disease) require more scrutiny than tests for high penetrance mutations.[177] It called on the FDA to give "particular attention" to the

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[168] Schwartz, "Genetic Testing and the Clinical Laboratory Improvement Amendments of 1988," 739.

[169] Centers for Disease Control and Prevention Public Health Practice Program Office, Division of Laboratory Systems, and DynCorp Health Research Services, *General Recommendations for Quality Assurance Programs for Laboratory Molecular Genetic Tests* (U.S. Department of Health and Human Services, August 31, 1999).

[170] Centers for Disease Control and Prevention, "Notice of Intent; Genetic Testing under the Clinical Laboratory Improvement Amendments," *Federal Register* 65 (2000): 25928. The notice defines human genetic testing to include testing that involves the analysis of chromosomes, DNA, RNA, and genes and gene products "to detect heritable or acquired disease-related disorders or conditions."

[171] Secretary's Advisory Committee on Genetic Testing website: *http://www4.od.nih.gov/oba/aboutsacgt.htm*, visited February 1, 2000.

[172] Secretary's Advisory Committee on Genetic Testing, *Adequacy of Oversight of Genetic Tests*, xx.

[173] It defines genetic testing as testing that "involves the analysis of chromosomes, DNA, RNA, genes, and/or gene products that is causing or is likely to cause a specific disease or condition" and which may be performed "for a number of purposes." Ibid., 1–2.

[174] Ibid., 22–23.

[175] Ibid., ii.

[176] Ibid., 13. For a discussion of social considerations, see ibid., 18.

[177] Ibid., 2, 26. For a discussion of gene penetrance, see Chapter 1, page 13.

review of predictive genetic tests that assess a healthy person's future disease risk in the absence of any preventive measures.[178] It also called on the Secretary to consider development of a mechanism outside FDA review to "ensure the identification, and appropriate review, of tests that raise major social and ethical concerns."[179]

The Secretary's Advisory Committee called for strengthening of CLIA regulation of genetic tests.[180] It agreed with the NIH-DOE Task Force on Genetic Testing that, for many tests, continued data collection is essential to assessment of clinical validity and utility. It recommended that relevant agencies of the Department of Health and Human Services (DHHS) work collaboratively with researchers and test developers to promote shared data collection, analysis, and dissemination.[181]

***Issues in New York's Genetic Testing Oversight***

In the course of this project, the Task Force staff solicited input from New York State-licensed physicians practicing as clinical geneticists and directors of laboratories permitted to perform genetic tests on specimens originating in New York. Many who responded indicated strong support for New York's oversight program, but some respondents noted some concerns.

- Disincentives to Participate — Some respondents maintain that the process of obtaining and maintaining New York State licensure is burdensome and expensive and that, as a result, some laboratories outside of New York State choose not to maintain licenses.[182] Consequently, physicians in New York State (and their patients) do not have access to these laboratories. Some respondents expressed concern that they and their patients are sometimes denied access to the laboratory that may be most qualified to perform a particular test. Others reported cases in which physicians were sometimes limited to laboratories that did not accept payment by Medicaid. Concerns about restricted access to testing laboratories are likely to continue because of several factors, including restricted laboratory coverage policies of managed care health plans[183] and the effect of patenting and exclusive licensing of genetic tests, which, in some cases, means that testing may be performed by only one laboratory.[184] While there are procedures for

[178] Secretary's Advisory Committee on Genetic Testing, *Adequacy of Oversight of Genetic Tests*, ii.
[179] Ibid., vi.
[180] Ibid., 22–23.
[181] Ibid., 21–22.
[182] See page 324, this chapter.
[183] See, e.g., H. F. L. Mark et al., "The Impact of Managed Care on Genetic Testing Laboratories in the United States," *Cytobios* 88 (1996): 43; NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 52.
[184] Particular DNA sequences, targets of DNA-based tests, may be patented. See American College of Medical Genetics, *Position Statement on Gene Patents and Accessibility of Gene Testing*, August 21, 1999, American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/pol-34.htm*, visited March 28, 2000.

obtaining approval to use unpermitted laboratories when no permitted laboratories perform the desired test, complying with those procedures is perceived as adding time and expense to the testing process.

- Timeliness of Program Responsiveness — Some respondents commented that New York's Laboratory Reference System did not always respond expeditiously to requests for test approval or permission to use an unpermitted laboratory, although the program attempts to maintain a twenty-four-hour response target.

- Difficulty Locating Information about Permitted Labs — It can be difficult for clinicians to identify which laboratories are permitted to perform particular tests. The New York State Department of Health's website lists all New York State-approved laboratories by category (e.g., genetic testing), but information about which tests are permitted by individual laboratories is not listed.[185] There is no listing by disorder and no search function. Published listings of permitted genetic tests and testing laboratories become rapidly dated. In some cases, commercial testing laboratories issue brochures outlining all available clinical laboratory tests, only a minority of which have been approved by the New York program. Clinicians receiving these brochures are likely to be unaware of which tests are approved.

  One genetic test for which clear laboratory testing information was made available is testing for BRCA1/BRCA2 gene mutations, which indicate susceptibility for breast and ovarian cancer. New York State-permitted providers of BRCA gene testing are listed as an appendix to clinical guidelines produced by the American College of Medical Genetics with funding from the New York State Department of Health. These guidelines also are posted on the departmental website,[186] but there has been no updating of this list.

- Lack of Clear Criteria or Process for Assessing Clinical Validity — Some genetics professionals have expressed concerns that the Laboratory Reference System's criteria for approving tests lack formalized, accessible guidelines and that some approval decisions have appeared inconsistent. Some also expressed concerns that some tests approved as investigational tests following their submission for program review without clinical validity data (e.g., Fragile X testing) should be designated as generally accepted and that designation as investigational can be a barrier to coverage of testing fees by third-party payers.[187]

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[185] Some laboratories produce brochures listing ten, twenty, or more tests offered, not all of which are permitted by New York. The same lists are readily accessible by GeneTests™, but in both cases, the viewer cannot tell which tests are permitted by New York State.

[186] *Genetic Susceptibility to Breast and Ovarian Cancer: Assessment, Counseling and Testing Guidelines*, Appendix XII, New York State Department of Health website: *http://www.health.state.ny.us/nysdoh/ cancer/obcancer/ append13.htm*, visited April 4, 2000.

[187] See page 324, this chapter.

- Inability to Keep Pace with Developments in the Field of Genetic Testing — With expanded development of genetic tests, the Laboratory Reference System resources may not be sufficient to ensure timely and effective oversight.[188]

**Ensuring Clinical Genetic Services and Public Education**

Public health agencies play an important role in ensuring access to appropriate clinical genetic services, including preventive services. The state public health agency is generally the central locus for ensuring, although not necessarily directly providing, appropriate and accessible clinical services. Federal agencies support these efforts by funding and other activities.

### Ensuring Access to Services

*Federal Agency Activities*

The Genetics Services Branch of MCHB promotes federal/state partnerships to support access to genetic services for pregnant women, mothers, and children.[189] Through national projects and the sponsorship of state projects, the Genetics Services Branch promotes strengthening of the public health infrastructure and access to services, including specialty treatment centers. For example, in 1999, it established a national Newborn Screening and Genetic Resource Center. It also supports the education of health care professionals and promotes genetic literacy of the general public.

*State Agency Activities*

About 50 percent of state public health agencies provide early intervention services for children with genetic conditions.[190] The resulting services are referred to as a "safety net" for the poor, disadvantaged, and handicapped. State agencies also can provide databases of accessible services, ensure that services are available through managed care plans, and aid providers and patients, regardless of financial status, when obtaining needed genetics services.

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[188] As of September 1999, for example, New York State had permitted DNA-based and biochemical genetic tests for approximately 55 disorders, while the GeneTests™ national database listed clinical testing for 334 disorders.

[189] See Maternal and Child Health Bureau website: *http://www.mchb.hrsa.gov/html*, visited May 11, 2000. See also page 312, this chapter.

[190] F. Desposito and C. Reid, "Clinical Genetic Services and Their Relevance to the Public Health," 64.

The New York State Department of Health has a Genetics Services Program that funds services at designated clinical centers.[191] The program provides competitive contracts to state genetics providers (mostly hospital-based) around the state; there are currently twenty-three centers funded in an expense-based manner. Services covered include cognitive services by genetic counselors, nurses, and social workers; space and supplies; and outreach costs (e.g., travel costs for patients or providers in satellite clinics). The state collects data on genetics services provided by these centers and promotes self-sufficiency of service providers by educating program billers on how to maximize third-party reimbursement for genetic services. It also educates third-party payers about, and works to promote coverage of, these services.

Between two-thirds and three-quarters of funded services are prenatal services, including counseling for maternal serum screening, amniocentesis, and carrier testing based on ethnic/racial risk profile.[192] Most of the remaining Genetics Services Program funds cover services to children with genetic disorders, including those identified by the Newborn Screening Program.[193] The state also has designated specialty care centers for specified genetic disorders, including cystic fibrosis, sickle cell disease, and heritable metabolic disorders such as PKU.[194] Other programs within the New York State Department of Health, including the Children with Special Health Care Needs Program, help link families of children needing genetic services with other service programs and federal, state, and local insurance programs.[195]

An important tool for guiding both health care providers and the general public to available health services is the Internet. The New York State Department of Health website offers information for consumers, providers, and researchers. However, the "Information for Consumers" section, which lists over thirty-five "click-on" topics including cancer, diabetes, heart disease, and communicable diseases, contains no references to genetic diseases or genetic testing. Information about the Special Health Care Needs Program is available, but there is no information about the Genetics Services Program.

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[191] The program goals and activities are outlined in *GENES Genetic Services Directory*, produced by the New York State Department of Health Genetics Services Program in May 1998. The directory lists New York State genetic service providers and institutions.

[192] Services covered generally exclude services by M.D. and Ph.D. professionals and laboratory test fees. Telephone interview with Katharine Harris, New York State Department of Health Genetics Services Program Coordinator, June 11, 1999. For a discussion of carrier testing for cystic fibrosis based on racial/ethnic background, see Chapter 5, page 119.

[193] See Chapter 6, page 150.

[194] See N.Y.C.R.R. §§ 69-1.1 (n),(m), 69-1.7.

[195] See New York State Department of Health Resource Directory for Children with Special Health Care Needs website: *http://www.health.state.ny.us/nysdoh/prevent/special/special.htm*, visited February 25, 2000; see also Chapter 6, page 150.

## Ensuring Genetics Education

### Federal Education Activities

The NHGRI and DOE ELSI Programs have both designated genetics education as a priority area.[196] Based on preliminary ELSI-funded surveys, the NHGRI ELSI program noted that "most members of the general population and most health professionals are not knowledgeable about genetics, genetic technologies and the possible ethical, legal, and social implications of having genetic information."[197]

Since 1991, DOE's ELSI Program has sponsored forty-six projects for general public and school-based education, including a number of projects for high school and college students. It also has funded a series of radio programs for the general public and a judicial education program that has provided basic science and ELSI orientation to over 1,200 judges.

In addition, the NHGRI's ELSI Program has funded an additional forty education grants, mostly focused on professional education, and two resource projects. One NHGRI-sponsored project is the National Coalition for Health Professional Education in Genetics (NCHPG), an interdisciplinary national organization that promotes health professional education and access to information about advances in human genetics.[198]

Other federal agencies are playing a direct or sponsorship role in educating both the general public and health care professionals about genetics and the implications of genetic testing. The CDC Office of Genetics and Disease Prevention promotes genetics education and information exchange among clinical and research professionals through its Human Genome Epidemiology Network website, HuGE Net.[199] It also sponsors other activities, including a short course for health professionals entitled "Genetics and Disease Prevention: A Scientific Basis for Public Health Action."[200] The National Center for Biotechnical Information (NCBI) at the National Library of Medicine and National Institutes of Health provides genetics informational and educational Internet sites to the

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[196] ELSI Planning and Evaluation Group, *A Review and Analysis of the Ethical, Legal, and Social Implications (ELSI) Research Programs*, 12–14, National Human Genome Research Institute website: *http://www.nhgri.nih.gov/About_NHGRI/Der/Elsi/elsinews.html*, visited May 24, 2000.

[197] National Human Genome Research Institute, "Ethical, Legal and Social Implications (ELSI) Program Areas," National Human Genome Research Institute website: *http://www.nhgri.nih.gov/About_NHGRI/Der/Elsi/high_priority.html*, visited January 27, 2000.

[198] National Coalition for Health Professional Education website: *http://www.nchep.org*, visited January 27, 2000.

[199] See page 315, this chapter.

[200] See Centers for Disease Control and Prevention website: *http://www.cdc.gov/genetics/temporary/course.htm*, visited July 12, 1999.

public.[201] Internet sites include an information site for the general public called *Genes and Disease*[202] and the Online Mendelian Inheritance of Man (OMIM) website,[203] providing an up-to-date database listing and describing all identified human genetic diseases for genetics health care professionals and researchers.

*State Education Activities*

State-sponsored genetics education programs can help promote education of the general public and the professional community. The Washington State Department of Health has been a leading example. In 1997, the department instituted a statewide genetics education plan to form partnerships to promote genetics knowledge in schools, medical practice, and the general community.[204] The plan attempts to identify informational needs, catalog ongoing educational activities, make recommendations for improved education, and implement those recommendations through statewide partnerships.

In the New York State Department of Health, the Genetics Education and Information Program located within the Division of Chronic Disease Prevention and Adult Health promotes public and professional education about the role of genetics in common complex disorders of adulthood. Most activities to date have focused on cancer genetics. One activity is an e-mail listserv providing information exchange among cancer genetics practitioners in the state.[205] The list informs participants, including geneticists, genetic counselors, public health administrators, advocates, and others about published articles, ongoing research projects, educational programs, and other activities that concern cancer genetics. Other educational activities are underway, including presentations to the department's Healthy Women Partnership program staff (which provides free mammography screening and cervical cancer screening to uninsured and underinsured women) and creation of an e-mail listerv that focuses on the role of genetics in adult chronic disease and will have a national focus.[206] The program director also serves as a liaison with national projects with the CDC and other groups.[207]

The New York State Department of Health also sponsored development by the American College of Medical Genetics of clinical guidelines for the management of congenital malformations of newborns[208] and for genetic testing for susceptibility to

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[201] See F. Ouellette, "Internet Resources for the Clinical Geneticist," *Clinical Genetics* 56 (1999): 179.
[202] Genes and Disease website: *http://www.ncbi.nlm.nih.gov/disease*, visited May 22, 2000.
[203] Online Mendelian Inheritance of Man website: *http://www.ncbi.nlm.nih.gov/Omim*, visited May 22, 2000. The website is produced at Johns Hopkins University and represents over three decades of work by geneticist Victor McKusick and his collaborators. Ouellette, "Internet Resources for the Clinical Geneticist," 182.
[204] Washington State Department of Health, *Washington State Genetics Education Plan* (Seattle, September 30, 1997).
[205] K. Greendale, "Cancer Genetic Services in New York State," *Ribbon Newsletter* 4 (Fall 1999); 4, 5.
[206] Telephone interview with Karen Greendale, Director of the New York State Department of Health Genetics Education and Information Program, August 9, 2000.
[207] Ibid.
[208] American College of Medical Genetics Foundation, *Evaluation of the Newborn with Single or Multiple Congenital Anomalies*, 1999, available on the New York State Department of Health website, *http:// www.health.state.ny.us/nysdoh/dpprd/exec.htm*, visited August 22, 2000.

breast and ovarian cancer.[209] Both guidelines were produced in 1999, distributed to 25,000 New York State primary care physicians and other nongenetics specialists,[210] and posted on the New York State Department of Health website, although no provisions were made for updating them.[211]

Also within the New York State Department of Health, The Wadsworth Center promotes public science education, including genetics education, by an annual series of lectures in Albany.[212] The Wadsworth Center also sponsors annual legislative workshops to update legislative and executive staff about scientific advances, including those in molecular genetics.[213]

*Other Education Activities*

Nongovernmental organizations also are seeking to increase public genetics literacy. For example, Stanford University's Human Genome Education Program is a collaborative project involving program staff, scientists, and local middle and high school teachers to provide and facilitate public education and outreach in biotechnology and genome science.[214] The Cold Spring Harbor Laboratory's DNA Learning Center trains teachers and provides genetic news, information, and a forum for discussion at the center and on its website.[215] The Science and Literacy Health Project of the American Association for the Advancement of Science, with funding from DOE, promotes public education about the scientific and ethical issues of the Human Genome Project in its publication *Your Genes, Your Choices*.[216] The Genetic Alliance, an international not-for-profit coalition of individuals, professionals, and genetic support organizations, serves as an informational resource network for those affected by or otherwise interested in genetic diseases.[217]

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[209] American College of Medical Genetics Foundation, *Genetic Susceptibility to Breast and Ovarian Cancer: Assessment, Counseling and Testing Guidelines*, 1999, available on the New York State Department of Health website: *http://www.health.state.ny.us/nysdoh/cancer/obcancer/contents.htm*, visited March 3, 2000.

[210] Greendale, "Cancer Genetic Services in New York State," 5.

[211] Ibid.; telephone interview with Karen Greendale, Director of the New York State Department of Health Genetics Education and Information Program, August 9, 2000.

[212] Wadsworth Center website: *http://www.wadsworth.org/educate.public.htm*, visited May 23, 2000.

[213] Ibid.

[214] Stanford's Human Genome Education Program website: *http://www-shgc.stanford.edu/bio-ed*, visited June 17, 1998.

[215] Cold Spring Harbor Laboratory DNA Learning Center website: *http://www.vector.cshl.org/about/Mission.html*, visited May 23, 2000.

[216] American Association for the Advancement of Science website: *http://www.ehrweb.aaas.org/her/books/index.htm*, visited January 27, 2000.

[217] Genetic Alliance website: *http://www.geneticalliance/org*, visited May 23, 2000.

Another important approach to public genetics education is to provide forums in which journalists can meet with scientists and other spokespersons. This approach is important, as most Americans generally seek health information through magazines, newspapers, television, and the radio.[218] The Gene Media Forum, a nonprofit, nonpartisan project of the S.I. Newhouse School of Public Communications at Syracuse University, promotes interactions between leading journalists, scientists, ethicists, and others through public discussion forums.[219]

## Conclusions and Recommendations

### Oversight of Genetic Testing by Federal and State Government Agencies

**Federal government agencies should strengthen their oversight of clinical laboratory genetic tests, including tests provided as services, to ensure that tests have adequate analytical and clinical validity. New York State should continue its oversight of clinical genetic testing laboratories and should re-examine its criteria and processes for test approval and laboratory oversight.**

Safe and effective clinical laboratory testing requires formal oversight. We agree with others that clinically available genetic testing, especially predictive genetic testing, warrants careful scrutiny. While oversight of all clinical laboratory testing is important, several factors warrant special attention to genetic tests at the current time. These factors include the special concerns of predictive genetic testing of apparently healthy individuals, the implications of reproductive genetic testing, widespread public misunderstanding and misperceptions about genetics, the inadequacy of current federal oversight of genetic testing, and the expected broad expansion of development of new genetic tests. With the expected development of many new and complex tests, many requiring postmarket data collection, oversight of genetic tests will likely be complex and costly. The federal government is the most appropriate locus for regulatory oversight and promotion of safe and efficacious testing.

As recommended by the NIH-DOE Task Force and the Secretary's Advisory Committee, the Secretary of Health and Human Services should designate the appropriate federal government agency to exercise oversight for genetic tests provided as services based on the tests' analytical and clinical validity. We agree with the New York State Department of Health's Laboratory Reference System that questions about a test's utility — its usefulness to the person tested, including its clinical usefulness — are best left to patients and their physicians. We also agree with the NIH-DOE Task Force on Genetic Testing, the CLIAC Working Group on Genetic Testing, and the Secretary's Advisory

[218] For a discussion, see Chapter 4, pages 89, 91.

[219] The Gene Media Forum, S.I. Newhouse School of Public Communications, Syracuse University Lubin House website: *http://genemedia.org*, visited July 20, 2000.

Committee that CLIA requirements for the oversight of genetic testing should be strengthened.

We recognize the important leadership role of New York State in clinical laboratory test evaluation and note that New York's Laboratory Reference System is the only program in the United States that currently assesses the clinical validity of genetic tests provided as services. In the absence of federal oversight of these tests, this program performs a valuable service for New York State citizens. The program's inclusion of a laboratory test's clinical validity — the ability of a test to determine who has or will get a particular disease — has been recognized as a model for national policy groups, including the NIH-DOE Task Force on Genetic Testing, in their considerations about how best to ensure safe and efficacious genetic testing.

The exercise of genetic testing oversight authority by New York State, however, also entails a responsibility to do so in a timely, accessible, and up-to-date manner. This will require considerable attention and resources as new and complex tests are developed. Specific proposals for the New York Program's oversight of genetic testing follow.

**Approval Process for Genetic Tests**

The New York State Department of Health's Laboratory Reference System, and its Clinical Testing Review Panel, should review proposed genetic tests expeditiously, within a specified time period. Approval decisions for individual genetic tests should be made on a case-by-case basis, based on analytical validity and clinical validity data for the test's intended use. The program also should require testing laboratories to provide educational materials to providers ordering the test.

It is essential that individuals who are considering genetic testing are well informed about the degree of a test's validity and utility based on the test's intended use, for example, for predictive versus diagnostic/confirmatory testing. For this reason, and based on evidence that pretest informational materials presented to health care providers are often inadequate and sometimes misleading, New York State regulations should be amended to require that laboratories with permits to perform genetic tests provide accurate and appropriate educational materials to aid physicians who order the tests. While such information is not a substitute for counseling and informed consent conducted by a qualified physician, it is an important step toward ensuring that the physician is up-to-date about the rapidly evolving and complex test-specific information for which the testing laboratory is an appropriate source.

Approval decisions should be made by a committee that can provide expertise while safeguarding proprietary information about a test. Formation of the program's

CTRP review panel, including at least two individuals from outside the department, is an improvement over decision-making by the program section head alone. It also is essential that the program, in assuming responsibility for oversight of laboratory tests, ensure that reviews are expeditious and are completed within a specified time period.

### Establishment of Criteria for Genetic Test Approval

**The New York State Department of Health should develop clear guidelines to delineate the assessment criteria the Laboratory Reference System will use for approval of genetic tests. The guidelines document should be open for public comment by interested parties, including genetic testing laboratories and clinical geneticists practicing in New York State, prior to adoption by the department.**

Special concerns about genetic testing, especially predictive genetic testing, led the Secretary's Advisory Committee to consider an array of factors involved in a test's clinical validity — its ability to determine relative risk for future disease development. These factors include: differences in clinical validity data for different test populations; different uses of a test, for example, for diagnostic versus predictive purposes; varying levels of a test's predictive power (for example, detection of differences in relative risk of two-fold versus ten-fold); and varying levels of a test's clinical sensitivity, depending on the test method and whether, for example, it tests for all possible DNA coding sequence mutations or just selected mutations. The Secretary's Advisory Committee also considered that determination of acceptable levels of a test's clinical predictive value might be influenced by other factors, such as the existence of an independent confirmatory test or a preventive health measure.

We recommend that the New York program follow the example of the Secretary's Advisory Committee, reconsider these issues surrounding clinical validation of predictive genetic tests, and produce a guidelines document that is open to public comment by interested parties, including genetic testing laboratories and clinical geneticists practicing in New York State. Consideration and discussion of general guidelines for case-by-case review would benefit the program, laboratories seeking review, and clinical geneticists. Members of the Wadsworth Center have taken a first step in addressing these issues in a public response document to the Secretary's Advisory Committee.[220]

If the New York program retains its current categorization of approved tests as generally approved and investigational, the guidelines also should address criteria and processes for moving tests from the investigational to the generally approved category.[221] For example, should movement of a test from investigational to generally approved

[220] Dr. Ann Willey et al., Wadsworth Center, New York State Department of Health, in a letter of public comment from the New York State Department of Health Wadsworth Center as part of public comment to the Secretary's Committee on Genetic Testing, February 14, 2000.

[221] See recommendation, page 342, this chapter.

status, which has implications for coverage by third-party payers, require the request of the test laboratory, even when there is a general professional consensus, for example, based on published research from other laboratories, that support the higher status? The guidelines also should address the content of informational materials for genetic tests provided to health care providers and patients.

**State Oversight of Laboratory Quality Assurance**

**The New York Laboratory Reference System should continue to require that permitted genetic testing laboratories meet specified certification, performance, and personnel standards and participate in quality assurance programs.**

New York's program should continue to ensure the accurate and reliable performance of all genetic tests and the qualifications of genetic testing laboratory personnel. Unless superseded by future revisions to CLIA that would render current practices, including laboratory inspections, superfluous, New York's oversight of laboratory quality assurance for genetic testing should continue. The costs of these measures are outweighed by the assurance of safe and effective testing for New York State residents.

**Establishment of a Genetic Testing Advisory Committee**

**The New York State Department of Health should create a genetic testing advisory committee, composed of departmental members and representatives of New York's clinical and diagnostic laboratory genetics community, to meet at least annually to review New York's Laboratory Reference System's genetic test approvals, the approval process, and outcomes. The committee also should serve as a sounding board for the clinical genetics and genetic laboratory communities and aid the department in its efforts to disseminate genetic testing information among health care providers.**

The New York Laboratory Reference System's review and approval process for genetic tests should, to the extent feasible, be subject to periodic discussion by clinical professionals and laboratories outside the New York State Department of Health who are directly affected by decisions. For predictive genetic testing, complex aspects of a test's clinical validity, affecting decisions about whom should be offered testing and what clinical options exist for different individuals, would benefit from an active dialogue among oversight program personnel, practicing clinicians, and those developing and offering clinical testing.

The New York State Department of Health should establish a panel of clinical geneticists and laboratorians to meet at least yearly to review, as feasible, approval criteria and to consider emerging issues such as multiplex testing or concerns about restrictions in testing access because of patent licensure issues. This process would allow those affected by program decisions to comment on the approval process, for example, decision turnaround time, composition of the CTRP panel, and outcomes. It also would promote dissemination of genetic test information within the clinical and laboratory communities.

### Categorization of Approved Genetic Tests

**For genetic test approval, the New York Laboratory Reference System should move from its current categories of test approval, "generally accepted" and "investigational," to a single category of approved tests in which test-specific limitations or restrictions that are important to patients, providers, and/or payers are noted. For example, approval should specify, when relevant, the need for ongoing data collection to establish a test's clinical validity for its intended application.**

We support the New York program's proposal to move from the current categories of permitted laboratory tests, generally approved and investigational, to a single approval category. This approach addresses concerns about restriction of third-party payer coverage of testing fees for tests that have some degree of established clinical validity but require continued data collection. This concern is especially relevant for predictive genetic tests for which comprehensive clinical validity data collection for different populations will generally require many years. Citation of a test's specific limitations and restrictions — for example, limited clinical validity data for particular populations, valid but low predictive value (e.g., increasing lifetime relative risk for a disease two-fold, from 5 percent to 10 percent), or lack of a preventive health measure — would provide useful information both to health care providers and to third-party payers making coverage decisions.

This approach, as suggested by the NIH-DOE Task Force on Genetic Testing and the Secretary's Advisory Committee, encourages new test development by promoting coverage of testing fees, as appropriate, during a period of ongoing data collection.

### Provider Access to State Oversight Information

**The New York State Department of Health should ensure that an up-to-date database listing of New York State-approved genetic tests and the laboratories authorized to perform them is readily accessible to health care providers in New York State.**

In assuming its role in the oversight of laboratory tests, the reference system has a responsibility to ensure up-to-date access to listings of permitted tests and laboratories. While concerns about current limits to the program's processes for listing, updating, and

sharing that information with health care providers are not limited to genetic testing, the fast-paced growth in the appearance of new genetic tests, which is likely to continue, raises special concerns. The format of the program's website listing of genetic tests is cumbersome, and information is not adequately up-to-date. Responsible health care providers wishing to remain compliant with the program provisions face, in at least some cases, an unreasonable burden to obtain program information.

One exception is the listing of laboratories permitted to perform BRCA gene testing for breast and ovarian cancer susceptibility in a guidelines document available on the New York State Department of Health website. This listing provides a model and, instituted generally for all genetic tests, would allow health care providers to search for permitted laboratories based on disease listing. Another model is the national GeneTests™ website that lists laboratory tests for over 400 disorders and is searchable by disease and laboratory. While we acknowledge the costs involved to establish and maintain such a listing, doing so is essential if New York State continues to exercise responsibility for genetic test oversight.

### Exemption from State Regulations for Laboratory Licensure

**New York's Public Health Law, which requires state licensure for all laboratories performing tests on specimens obtained in New York, should be amended to permit the New York State Department of Health to grant exemptions on a case-by-case basis.**

The number of new genetic tests has increased steadily in recent years and many, including the Secretary's Advisory Committee, expect this increase to continue. Currently, clinical laboratory tests for over 400 disorders are available nationally, but New York's reference system has granted permits for only a minority of these tests. This disparity is likely to continue and may be exacerbated by factors, including disincentives for some out-of-state laboratories to seek New York State licensure, lack of knowledge about New York's program, restricted laboratory coverage by managed care health plans, and exclusive patenting and licensure of genetic tests.

Some of these factors, and the rarity of some disorders for which genetic testing is offered, have already prompted the program to authorize a process by which physicians may request to use a testing laboratory that does not hold a program permit for that test. This exemption, however, is not explicitly authorized by the New York State Public Health Law. [222] The law should be amended to authorize such departmental exemptions as appropriate.

[222] N.Y. Pub. Health Law § 574 (McKinney 1999).

It is also essential that New York's program review and grant such exemptions, as appropriate, in a defined and expeditious manner.

**Ongoing Collection, Evaluation, and Dissemination of Clinical Data**

**Federal and state health agencies should work with laboratories, providers, and other partners to promote the ongoing collection, evaluation, and dissemination of clinical validity and utility data for predictive genetic tests.**

Predictive genetic susceptibility tests that determine probabilistic disease risk information for healthy individuals differ from many other laboratory tests in that establishment of clinical validity can take years of continued data collection and analysis. For predictive genetic tests, including those that can predict future disease with near 100 percent certainty, useful measures to prevent or minimize disease often are inadequate or nonexistent.

We agree with the NIH-DOE Task Force on Genetic Testing and the Secretary's Advisory Committee that oversight mechanisms must be flexible enough to promote test development and continued data collection, sharing, analysis, and dissemination. Federal and state government agencies should promote relationships with other partners, including nonprofit and commercial organizations for test research, development, and marketing, to perform this important function. Examples such as Myriad Genetics' collaboration with the National Cancer Institute for BRCA gene testing and research follow-up and the New York State Department of Health's sponsorship of clinical guidelines for BRCA gene testing should be replicated and extended.

**Role of Institutional Review Boards**

**Organizations seeking New York State approval for genetic tests that require ongoing collection of clinical data should be required to submit evidence that they have obtained approval of an institutional review board.**

Predictive genetic tests often require continued data collection from tested individuals to establish optimal clinical validity data. For all such tests, the New York program should require evidence that the entity seeking approval to market the test clinically has undergone local review and obtained approval of the test protocol's data collection process by its own IRB. As recommended by the NIH-DOE Task Force on Genetic Testing, IRB review should include consideration of whether the scientific merits of the protocol warrant the risks posed to those who are tested and asked to participate in the follow-up investigative studies.

### Assessment of Population Needs

**Federal and state health agencies play an important role in assessing the population's genetic and environmental risk factors. The New York State Department of Health should continue its activities in statewide assessment of the population's genetic health and genetic epidemiology research.**

Surveillance of population health and disease indicators, coupled with other epidemiologic research, can provide powerful information about both genetic and environmental factors that contribute to disease morbidity and mortality. Surveillance activities of the New York State Department of Health, including its Congenital Malformations Registry and Cancer Registry, are potentially valuable sources of information about factors that impair health. They also can point to shortcomings in public health strategies to prevent disease or promote early disease detection (e.g., breast cancer screening by mammography) within the general population or in particular demographically defined populations.

The technologies and information resulting from the Human Genome Project provide new and exciting possibilities for molecular epidemiology research to analyze the role of inherited genetic variants in susceptibility to common complex disorders such as asthma, cancer, and cardiovascular disease and to environmental health hazards. These new possibilities pose both opportunities and responsibilities for public health agencies to promote research and disease prevention without causing individual and social harms that can result from misguided projects and tissue sample use (including newborn bloodspot use), as discussed in earlier chapters.[223] We support the genetic epidemiology research studies of the New York State Department of Health, which appear to include appropriate measures to ensure the responsible use of research samples and demographic data.

The New York State Department of Health also should continue to monitor the population's need for genetic services, through its surveillance activities and by working to ensure access to needed clinical services. It should continue to ensure accessible genetics service centers for prenatal care and care of newborns, children, and adults with genetic disorders. It also should turn its attention to ensuring adequate access, as medically appropriate, to counseling and testing services for the new class of predictive susceptibility genetic testing (e.g., breast and ovarian cancer susceptibility testing).

### Public and Provider Education

**Federal and state health agencies play an important role in educating the public about genetics generally and about particular genetics**

[223] See Chapter 7, page 196; Chapter 6, page 156.

**services that are available to the public. They also should support production and dissemination of genetics educational materials to health care providers.**

Many of the fears surrounding genetic testing and the potential harms of testing discussed in this report are caused by misunderstanding and misinterpretation of genetics and genetic test information by the general public and health care professionals. Public health agencies have an important role in promoting education about the science of genetics and the Human Genome Project and its ethical, legal, and social implications. We strongly support governmental and nongovernmental efforts to promote genetic literacy in schools, the general community, and the health care community.

An important tool to promote genetic literacy is the Internet. Health agencies, including the New York State Department of Health, should promote the use of agency websites to disseminate educational and program information about genetics for the public and health care providers. Because of the rapid pace of scientific and clinical genetics research, it also is essential that all educational information, including clinical guidelines to aid health care providers in the provision of genetic testing and other services, are kept up-to-date.

### Coordination of State Agency Genetics Activities

**The New York State Department of Health should assure coordination of activities of departmental personnel and programs that promote genetics health and research activities throughout the department. The department also should promote coordination of its efforts with those of other partners outside the department.**

The Human Genome Project has ushered in a new era of genetics, with profound implications for clinical and public health genetics practices. While continuing to ensure activities and services for congenital malformations and single-gene diseases such as PKU and sickle cell disease, public health agencies need to widen their programmatic approaches to genetics in access, policy, and assurance activities. The New York State Department of Health has taken an important step toward integrating genetics into its Division of Chronic Disease Services. It should take further steps to ensure the coordination of all genetics-related programs and activities within the department and to promote the integration of genetic literacy into all appropriate programs. Approaches to ensure such coordination may include appointment of a departmental genetics coordinator and/or creation of an agency-wide genetics committee.

# 12

# Integrating Genetics Services into Clinical Care

# Genetics Services Delivery Systems: An Overview

## What Are Genetics Services?

Clinical genetics services encompass a wide application of genetics technology in analyzing human DNA, RNA, chromosomes, proteins, or certain metabolites. These services can include genetic testing, assessment of risk based on family and personal history, interpretation of genetic test results, pretest and posttest genetic counseling, treatment and management of genetic disorders, and DNA banking for possible testing in the future.[1] Clinical genetic testing includes diagnostic testing to confirm the diagnosis of a medical condition with a genetic component based on an individual's symptoms, as well as several categories of predictive testing, such as newborn screening tests, reproductive testing, and testing of individuals for late-onset disorders.[2] An essential component of all genetics services is genetic counseling, which is an educational process that assists the patient and family members in assessing, understanding, and dealing with the risk of a genetic disorder occurring within a family, the results of genetic tests, and the treatment and management of a genetic disorder.[3]

## Genetics Services Settings

Until recently, genetics services were provided primarily by specially trained health professionals in institutional medical settings, such as university hospitals and public health clinics.[4] As a result of the growth in medical genetics, genetics services are

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[1] See GeneTests™, "Genetic Counseling and Testing," website: *http://www.genetests.org*, visited September 30, 1999; R. E. Pyeritz, "Medical Genetics: End of the Beginning or Beginning of the End?" *ACMG Presidential Address* 1, no. 1 (1998): 56, 58–59; S. J. Hayflick and M. P. Eiff, "Role of Primary Care Providers in the Delivery of Genetic Services," *Community Genetics* 1 (1998): 18, 19; N. Touchette et al., *Toward the 21st Century — Incorporating Genetics into Primary Health Care* (Plainview, NY: Cold Spring Harbor Laboratory Press, 1997): 16.

[2] See Chapter 2 for discussion of the types and uses of genetic testing.

[3] Touchette et al., *Toward the 21st Century*, 16.

[4] D. H. Lea, J. F. Jenkins, and C. A. Francomano, *Genetics in Clinical Practice: New Directions for Nursing and Health Care* (Sudbury, MA: Jones and Bartlett Publishers, 1998), 17; R. Blatt, "Medical Genetic Services: What They Are and Where to Find Them," *The Gene Letter* (July 1996), website: *http://www.geneletter.org*, visited March 30, 1999; J. A. Scott et al., "Genetic Counselor Training: A Review and Considerations for the Future," *American Journal of Human Genetics* 42 (1988): 191, 197; P. Reilly, *Genetics, Law and Social Policy* (Cambridge, MA: Harvard University Press, 1977), 175. This was because academic medical settings received federal funding to provide genetics services. Since the passage of the National Genetic Diseases Act in 1976, Title IV of P.L. 94-278, the Genetics Services Branch of the Maternal and Child Health Bureau, a branch of the U.S. Department of Health and Human Services, has allocated federal funding to ensure access to comprehensive genetics services for all populations. Lea, Jenkins, and Francomano, *Genetics in Clinical Practice*, 17; R. Blatt, "Public Health Genetics: The Role of

increasingly being delivered in other settings, such as private hospitals, managed health care organizations, physicians' private practices, commercial laboratories, community hospitals, state or federal departments of health, rural outreach programs, and private practice.[5] Traditionally, genetics services focused primarily on relatively rare prenatal, newborn, and pediatric disorders — mostly single-gene disorders[6] and congenital malformations. As a result of recent genetic discoveries and new testing technologies, however, there is a growing interest in predictive genetic testing of healthy adults for late-onset disorders, including predictive testing to determine cancer susceptibility. Thus, genetics services may be specialized by age group (e.g., prenatal, pediatric, adult) or by medical condition (e.g., cancer genetics).[7]

**Genetics Services Providers**

Both genetics professionals and nongenetics health professionals provide genetics services to patients and other health care providers.

***Genetics Professionals***

Genetics professionals have special training in genetics and provide specified genetics services directly or indirectly, through other health care providers, to patients. Their responsibilities may include: (a) obtaining and interpreting complex family history information, (b) providing detailed explanations of genetic testing, (c) diagnosing children or adults, (d) prenatal diagnosis, (e) providing further information regarding protection of patient privacy, (f) interpreting complicated genetics test results, (g) genetic counseling, (h) testing individuals or families who are known to be at higher risk, and (i) screening entire populations or groups.[8]

Genetics professionals include medical geneticists, Ph.D. clinical geneticists, genetic counselors, and genetic nurse specialists.[9] They come from a multitude of specialty areas, including obstetrics, gynecology, pediatrics, and internal medicine, and they work primarily in an interdisciplinary team to provide genetics-based health care.[10] In most clinical genetics programs, the core providers are clinical geneticists (physicians with subspecialty training in clinical genetics) and genetic counselors.[11] Genetics professionals tend to be clustered in the Northeast and on the West Coast, with a heavy

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State Genetics Programs," *The Gene Letter* (January 1997), website: *http://www.geneletter.org*, visited March 30, 1999. See Chapter 11, page 312, for discussion of the federal genetics program known as CORN.

[5] Lea, Jenkins, and Francomano, *Genetics in Clinical Practice*, 17–18; Touchette et al., *Toward the 21st Century*, 27; Blatt, "Medical Genetic Services," website: *http://www.geneletter.org*; Scott et al., "Genetic Counselor Training," 197.

[6] See Chapter 1, page 14.

[7] GeneTests™, "Genetic Counseling and Testing," website: *http://www.genetests.org*.

[8] Lea, Jenkins, and Francomano, *Genetics in Clinical Practice*, 18; D. C. Wertz, "Society and the Not-So-New Genetics: What Are We Afraid Of? Some Future Predictions From a Social Scientist," *Journal of Contemporary Health Law and Policy* 13 (1997): 299, 305.

[9] Lea, Jenkins, and Francomano, *Genetics in Clinical Practice*, 17.

[10] Ibid., 17–18; Blatt, "Medical Genetic Services," website: *http://www.geneletter.org.*

[11] B. A. Bernhardt and R. E. Pyeritz, "The Organization and Delivery of Clinical Genetics Services," *Pediatric Clinics of North America* 39, no. 1 (1992): 1, 10.

concentration in California, Illinois, New Jersey, New York, and Pennsylvania.[12] The American Society of Human Genetics (ASHG), a nonprofit professional society founded in 1948, serves as the primary scientific and professional society for all human geneticists in North America.[13] Its over 5,000 members include researchers, academicians, clinicians, laboratory practice professionals, genetic counselors, nurses, and others involved in human genetics.[14] In addition, the Genetics Society of America, founded in 1931, represents scientists and academicians interested in the broad field of genetics studies and supports research and education in genetics.[15]

### *Nongenetics Health Professionals*

With advances in genetics technology and the growing demand for genetics services, nongenetics health professionals — such as primary care physicians, specialist physicians, general nurse practitioners, and social workers — are increasingly involved in providing certain genetics services to patients. For example, primary care physicians and some specialist physicians, such as oncologists, obstetrician-gynecologists, and neonatologists, are increasingly incorporating some genetics services into their primary or specialty practice.

## Nondirectiveness

Traditionally, genetics professionals used a "nondirective" approach — a primarily educational process in which they inform their clients of the risks and benefits of testing and interpret test results, but insist that clients make their decisions independently.[16] The nondirective approach originated in response to the eugenic misuse of genetic information during the early part of this century.[17] To avoid influencing clients' decisions, nondirective genetics professionals focus on medical information, communicate in terms that are as value-neutral as possible, and offer unconditional support for clients' choices.[18] Most discussions of nondirectiveness have focused on prenatal testing and reproductive decision-making,

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[12] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks: Implications for Health and Social Policy*, ed. L. B. Andrews et al. (Washington, D.C.: National Academy Press, 1994), 203.

[13] Ibid., 204; American Society of Human Genetics, "ASHG Objectives and Benefits," website: *http://www.faseb.org/genetics/ashg/org/obj-bene.htm*, visited July 1, 1999.

[14] American Society of Human Genetics, "ASHG Objectives and Benefits," website: *http://www.faseb.org/genetics/ashg/org/obj-bene.htm*.

[15] Genetics Society of America, "About the Genetics Society of America," website: *http://www.faseb.org/genetics/gsa/gsa-int.htm*, visited July 2, 1999.

[16] M. T. White, "Making Responsible Decisions: An Interpretive Ethic for Genetic Decisionmaking," *Hastings Center Report* 29, no. 1 (1999): 14, 15–16; President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions* (Washington, D.C.: U.S. Government Printing Office, February 1983), 37.

[17] For a discussion of eugenics, see Chapter 4, page 80.

[18] White, "Making Responsible Decisions," 16.

which have been the primary areas for genetics services for the past 20 years.[19] In one study, a majority of the counseling clients perceived the genetic counselors as nondirective and reported that they liked this style and/or that they regarded it as essential.[20] However, there is a lack of agreement about the definition of nondirectiveness and whether nondirectiveness is the appropriate type of communication to facilitate all genetics services, especially with the increasing availability of presymptomatic or predisposition testing for adult-onset disorders.[21] Recent studies conclude that genetics professionals struggle with the concept of nondirectiveness and that genetic counseling sessions are, in fact, not purely nondirective interactions.[22]

## Genetic Specialists

The field of medical genetics has expanded so rapidly that specialty areas within the field have emerged: clinical genetics, medical genetics, and laboratory genetics (clinical cytogenetics, clinical biochemical, and clinical molecular genetics).[23] The American Board of Medical Genetics (ABMG) defines a clinical geneticist as an individual who holds an M.D. or D.O. degree, has had two years in an accredited clinical residency program in another medical specialty and two years in an accredited residency in clinical genetics, has a valid medical license, and "has demonstrated competence to provide comprehensive genetic diagnostic, management, therapeutic, and counseling services."[24] A Ph.D. medical geneticist is an individual with a U.S.-earned Ph.D. degree in genetics, human genetics, or a related field who "demonstrates competence to provide comprehensive genetic diagnostic, management, and counseling services, as well as expertise in complex risk assessments and in the integration of clinical and genetic information."[25] Ph.D. medical geneticists might work in a team of clinical specialists or as consultants in clinical or legal settings, counsel patients and families at risk for genetic disorders, or supervise management of medical genetics programs.[26]

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[19] B. A. Bernhardt, "Empirical Evidence That Genetic Counseling Is Directive: Where Do We Go from Here?" *American Journal of Human Genetics* 60 (1997): 17, 18.

[20] P. M. Veach et al., "Client Perceptions of the Impact of Genetic Counseling: An Exploratory Study," *Journal of Genetic Counseling* 8, no. 4 (1999): 191, 208.

[21] See G. Anderson, "Nondirectiveness in Prenatal Genetics: Patients Read between the Lines," *Nursing Ethics* 6, no. 2 (1999): 126, 128 (study shows that it is a misconception to equate nondirectiveness with protecting or fostering autonomous decision-making); A. McConkie-Rosell and J. A. Sullivan, "Genetic Counseling — Stress, Coping, and the Empowerment Perspective," *Journal of Genetic Counseling* 8 (1999): 345, 346–347 (proposing a model for genetic counseling incorporating empowerment and nondirectiveness into a theoretical framework for genetic counseling intervention); White, "Making Responsible Decisions," 14; Bernhardt, "Empirical Evidence That Genetic Counseling Is Directive," 18; D. C. Wertz, "Reconsidering 'Nondirectiveness' in Genetic Counseling," *The Gene Letter* (January 1997), website: *http://www.geneletter.org*, visited March 30, 1999.

[22] See McConkie-Rosell and Sullivan, "Genetic Counseling," 347.

[23] American Board of Medical Genetics, "General Information about the ABMG," website: *http://www.faseb.org/genetics/abmg/general.htm*, visited July 1, 1999.

[24] American Board of Medical Genetics, "Certification Examination Program: Description of Specialties in Medical Genetics," website: *http://www.faseb.org/genetics/abmg/99-14.htm*, visited July 1, 1999.

[25] Ibid.

[26] American Board of Medical Genetics, "Certification Examination Program: Subject Outlines," website: *http://www.faseb.org/genetics/abmg/99-19.htm*, visited July 1, 1999.

## Professional Certification in Medical Genetics

The ABMG was founded in 1980 under the sponsorship of the ASHG and joined the American Board of Medical Specialties (ABMS) in 1991.[27] The ABMG prepares and administers examinations to certify individuals who provide services in medical genetics and accredits training programs in the field of human genetics.[28] The ABMG offers certification in clinical genetics, Ph.D. medical genetics, clinical cytogenetics, clinical biochemical genetics, and clinical molecular genetics.[29] The ABMG's certification examinations are offered every three years.[30] Beginning with the 1993 certification examination, all certificates are time-limited for a period of ten years from the date of the examination.[31]

The certification examinations consist of a general (core) examination and specialty examinations in the following areas: (a) clinical genetics, (b) Ph.D. medical genetics, (c) clinical cytogenics, (d) clinical biochemical genetics, and (e) clinical molecular genetics.[32] All applicants must take the general examination and at least one specialty examination.[33] In order to be eligible to take the examination, the candidate must have successfully completed a minimum of two years in an ABMG-accredited

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[27] American Society of Human Genetics, "Overview of Human Genetics Organizations," website: *http://www.faseb.org/genetics/ashg/geneintr.htm*, visited February 15, 2000.

[28] American Board of Medical Genetics, "Certification Examination Program: Purpose of ABMG," website: *http://www.faseb.org/genetics/abmg/99-03.htm*, visited July 1, 1999.

[29] American Board of Medical Genetics, "Certification Examination Program: Description of Specialties in Medical Genetics," website: *http://www.faseb.org/genetics/abmg/99-14.htm*, visited July 1, 1999. Until 1993, the American Board of Medical Genetics also offered certification for the subspecialty in genetic counseling. However, when the ABMG joined the ABMS in 1991, it was required to stop certifying master's-level genetics counselors because the ABMS's policy is to admit only boards that certify doctoral-level individuals. American Board of Medical Genetics, "General Information about the ABMG," website: *http://www.faseb.org/genetics/abmg/general.htm*; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 213–214. Consequently, the master's degree-level genetic counselors formed an independent board, the American Board of Genetic Counseling to certify genetic counselors and to accredit graduate level training programs. See page 355, this chapter.

[30] American Board of Medical Genetics, "General Information about the ABMG," website: *http://www.faseb.org/genetics/abmg/general.htm*. The most recent set of examinations was offered in June 1999. American Board of Medical Genetics, "Certification Examination Program: Schedule of Examinations," website: *http://www.faseb.org/genetics/abmg/99-21.htm*, visited July 1, 1999.

[31] American Board of Medical Genetics, "Time-Limited Certification," website: *http://www.faseb.org/genetics/abmg/time_lim.htm*, visited July 1, 1999. The ABMG is considering requirements for recertification. Ibid.

[32] American Board of Medical Genetics, "Certification Examination Program: Specialty Examination Offered," website: *http://www.faseb.org/genetics/abmg/99-04.htm*, visited July 1, 1999.

[33] Ibid.

training program.[34] Applicants are required to pass the certification examination within two successive examination cycles or within six years of application, whichever comes first.[35] As of December 1999, there were 2,191 ABMG diplomates in the following specialty areas: clinical genetics (1,006), Ph.D. medical genetics (150), clinical biochemical genetics (180), clinical biochemical/molecular genetics (49), clinical cytogenetics (522), and clinical molecular genetics (284).[36]

Many commentators believe that there are not enough medical geneticists with clinical training to meet the growing demand for clinical genetics services.[37] Data from the early 1990s indicate that most Ph.D.-level geneticists enter research or laboratory careers rather than clinical genetics settings.[38] Moreover, of those M.D.s who complete their training in genetics, most are in pediatrics, followed by internal medicine and obstetrics.[39] As genetic testing becomes more widely available, there may not be enough physicians outside these specialties with training to provide the necessary specialized genetics services.[40]

**Accreditation of Medical Genetics Training Programs**

To ensure that standards and practices are maintained at the institutional level, the ABMG developed a process of accrediting programs that train medical genetics personnel

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[34] American Board of Medical Genetics, "General Information about the ABMG," website: *http:// www.faseb.org/genetics/abmg/general.htm*. Once the application has been approved, the applicant is considered an active candidate for ABMG certification. The term "board-eligible" is not used to describe this status. American Board of Medical Genetics, "Certification Examination Program: Specialty Examination Offered," website: *http://www.faseb.org/genetics/abmg/99-04.htm*.

[35] American Board of Medical Genetics, "Certification Examination Program: Specialty Examination Offered," website: *http://www.faseb.org/genetics/abmg/99-04.htm*.

[36] E-mail correspondence with Sharon Robinson, M.S., ABMG/ABGC Administrator, American Board of Genetic Counseling, Bethesda, MD, December 23, 1999; see American Board of Medical Genetics, "ABMG Diplomates Listing — Clinical Genetics," website: *http://www.faseb.org/genetics/abmg_cg.htm*, visited December 22, 1999; American Board of Medical Genetics, "ABMG Diplomates Listing — PHD Medical Genetics," website: *http://www.faseb.org/genetics/abmg_phdmg.html*, visited December 22, 1999; American Board of Medical Genetics, "ABMG Diplomates Listing — Clinical Biochemical Genetics," website: *http:// www.faseb.org/genetics/abmg_cbg.html*, visited December 22, 1999; American Board of Medical Genetics, "ABMG Diplomates Listing — Clinical Biochemical/Molecular Genetics," website: *http://www.faseb.org/ genetics/abmg_cbmg.html*, visited December 22, 1999; American Board of Medical Genetics, "ABMG Diplomates Listing — Clinical Cytogenetics," website: *http://www.faseb.org/genetics/ abmg_cc.html*, visited December 22, 1999; American Board of Medical Genetics, "ABMG Diplomates Listing — Clinical Molecular Genetics," website: *http://www.faseb.org/genetics/abmg_cmg.html*, visited December 22, 1999.

[37] See F. S. Collins, "Shattuck Lecture — Medical and Societal Consequences of the Human Genome Project," *New England Journal of Medicine* 341 (1999): 28, 35; Pyeritz, "Medical Genetics: End of the Beginning," 58; F. S. Collins, "Preparing Health Professionals for the Genetic Revolution," *Journal of the American Medical Association* 278 (1997): 1285; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 205–206.

[38] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 205–206.

[39] Ibid.

[40] Ibid.

in the areas of clinical and laboratory medicine.[41] Until the end of 1997, the ABMG accredited all training programs.[42] Since 1998, the Residency Review Committee for Medical Genetics of the Accreditation Council for Graduate Medical Education has accredited clinical genetics training programs.[43] The ABMG continues to accredit Ph.D. medical genetics training programs and laboratory training programs (clinical biochemical genetics, clinical cytogenics, and clinical molecular genetics).[44]

### Professional Associations

In 1991, clinical practitioners of medical and laboratory genetics formed the American College of Medical Genetics (ACMG) and the American College of Medical Genetics Foundation (ACMGF) to represent the profession of medical genetics.[45] In 1995, the ACMG became a full member of the Council of Medical Specialty Societies.[46] In 1996, the ACMG was granted a seat in the House of Delegates of the American Medical Association (AMA).[47] The ACMGF is organized to support research, education, and knowledge in the field of medical genetics, with the objective of advancing the science of medical genetics and fulfilling the medical genetic needs of the public.[48]

## Genetic Counselors

### Who Are Genetic Counselors?

Genetic counselors are "health professionals who are academically and clinically prepared to provide genetic counseling services to individuals and families seeking information about the occurrence, or risk of recurrence, of a genetic condition or birth defect."[49] They communicate "genetic, medical, and technical information in a comprehensive, understandable, nondirective manner with knowledge of and insight into

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[41] American Board of Medical Genetics, "General Information about the ABMG," website: *http://www.faseb.org/genetics/abmg/general.htm*.
[42] American Board of Medical Genetics, "ABMG Requirements for Accreditation and Reaccredidation," website: *http://www.faseb.org/genetics/abmg/accreql.htm*, visited July 1, 1999.
[43] Ibid.
[44] Ibid.
[45] American Society of Human Genetics, "Overview of Human Genetics Organizations," website: *http://www.faseb.org/genetics/ashg/geneintr.htm*, visited July 1, 1999.
[46] American College of Medical Genetics, "Association Information," website: *http://www.faseb.org/genetics/acmg/associat.htm*, visited July 1, 1999.
[47] Ibid.
[48] American College of Medical Genetics, "ACMG Foundation," website: *http://www.faseb.org/genetics/acmg/acmg-f00.htm*, visited July 1, 1999.
[49] American Board of Genetic Counseling, "Certification Examination Program: Competencies," website: *http://www.faseb.org/genetics/abgc/99-05.htm*, visited May 3, 1999.

the psychosocial and ethnocultural experiences important to each client . . . and family."[50] Genetic counselors provide counseling in various medical specialty areas, the most common being prenatal care, followed by pediatrics and oncological care.[51] Other specialty areas of genetic counselors include adult medicine, screening, neurogenetics, molecular/cytogenetic testing, and newborn screening.[52]

### Components of Genetic Counseling

Genetic counseling, which may occur both before and after testing, includes:[53]

- Eliciting and interpreting individual and family medical, developmental, and reproductive histories
- Determining the mode of inheritance and risk of occurrence and recurrence of genetic conditions and birth defects
- Explaining the etiology, natural history, diagnosis, and management of these conditions
- Interpreting and explaining the results of genetic tests and other diagnostic studies
- Performing a psychosocial assessment to identify emotional, social, educational, and cultural issues
- Evaluating the client's and/or family's responses to the condition or risk of occurrence
- Providing client-centered counseling and anticipatory guidance
- Promoting informed decision-making about testing, management, reproduction, and communication with family members
- Identifying and using community resources that provide medical, educational, financial, and psychosocial support and advocacy

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[50] American Board of Genetic Counseling, "Requirements for Graduate Programs in Genetic Counseling Seeking Accreditation: Description of the Professional," website: *http://www.faseb.org/genetics/abgc/acc-02a.htm*, visited May 4, 1999.

[51] National Society of Genetic Counselors, "Professional Status Survey 1998," *Perspectives in Genetic Counseling Supplement* 20, no. 1 (1998): S3.

[52] Ibid.

[53] Ibid.; Randi Zinberg, M.S., Genetic Counselor, Department of Human Genetics, Mount Sinai School of Medicine of the New York University, New York, NY, presentation to the New York State Task Force on Life and the Law, May 26, 1999. See, e.g., D. Diekmann-Tapon, "Case Report: Object Relations Family Therapy as a Model for Genetic Counseling," *Journal of Genetic Counseling* 8, no. 4 (1999): 235.

- Providing written documentation of medical, genetic, and counseling information for families and other health professionals

Genetic counselors spend an average of one hour in counseling new families and one-half hour for returning families.[54] However, many genetic counselors report that the total amount of time spent per client — often many hours — is much greater than the counseling session alone because it includes research, preparing reports, interviewing the clients' family members, collecting several generations of family histories, collecting medical histories, conferring with the clients' primary care physician or health care specialists, and various administrative tasks.[55]

**Genetic Counseling as a Profession**

In 1969, the first master's-level training program in genetic counseling was established at Sarah Lawrence College in New York.[56] As of May 2000, twenty-six training programs in the United States offer master's degrees in genetic counseling, two of them in New York — Sarah Lawrence College in Bronxville and Mount Sinai School of Medicine of the New York University.[57] Genetic counseling training programs include both didactic courses and clinical training, which together seek to develop skills in communication, critical thinking, interpersonal relations, counseling, and psychosocial assessment, as well as to instill professional ethics and values.[58] Students participate in supervised clinical rotations and internships throughout their training.[59] Over 90 percent of recent graduates found work within six months of graduation.[60]

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[54] B. A. Bernhardt et al., "The Economics of Clinical Genetics Services: II. A Time Analysis of a Medical Genetics Clinic," *American Journal of Human Genetics* 41 (1987): 559, 562; see also D. C. Wertz, "Risk Estimation and Length of Counseling," *GeneLetter* (August 1997), website: *http://www.geneletter.com*, visited July 17, 2000 (a small observational study of genetic counseling in England reported that the average consultation lasted twenty-eight minutes).

[55] See J. Kling, "Genetic Counseling: The Human Side of Science," *The Scientist* 13, no. 15 (1999): website: *http://www.the-scientist.library.upenn.edu/yr1999/july/prof_990719.html*, visited July 16, 1999; Meeting of genetic counselors with Task Force staff on May 5, 1999.

[56] Scott et al., "Genetic Counselor Training," 191.

[57] American Board of Genetic Counseling, "Genetic Counseling Training Programs Accredited by the ABGC," website: *http://www.faseb.org/genetics/abgc/tr-prog1.htm*, visited May 3, 2000; National Society of Genetic Counselors website: *http://www.nsgc.org/careers.html*, visited May 3, 1999.

[58] American Board of Genetic Counseling, "Requirements for Graduates in Genetic Counseling Seeking Accreditation," website: *http://www.faseb.org/genetics/abgc/acc-04a.htm*, visited July 1, 1999; American Board of Genetic Counseling, "Requirements for Graduates in Genetic Counseling Seeking Accreditation," website: *http://www.faseb.org/genetics/abgc/acc-04b.htm*, visited July 1, 1999.

[59] Randi Zinberg, M.S., Genetic Counselor, Department of Human Genetics, Mount Sinai School of Medicine of the New York University, New York, NY, presentation to the New York State Task Force on Life and the Law, May 26, 1999.

[60] Ibid.

Before 1993, the ABMG administered certification examinations in genetic counseling.[61] In 1993, the American Board of Genetic Counseling (ABGC) was established to prepare and administer examinations to certify individuals in genetic counseling and to accredit master's degree programs in genetic counseling.[62] To obtain ABGC certification, genetic counselors must complete one of the accredited programs[63] and pass a comprehensive certifying examination comprising a general genetics exam (the same exam given by the ABMG to medical geneticists) and a specialty examination in genetic counseling.[64] In December 1999, there were 1,410 board-certified genetic counselors.[65]

The National Society of Genetic Counselors (NSGC), the professional society for master's-level genetic counselors, adopted a professional code of ethics for genetic counselors in 1991.[66] The code affirms that genetic counselors should strive to acquire all relevant information, continue their education and training, keep abreast of current standards of practice, and recognize the limits of their own knowledge and expertise.[67] Regarding the client-counselor relationship, the code requires that genetic counselors serve all clients equally; respect their clients' beliefs, cultural traditions, inclinations, circumstances, and feelings; enable their clients to make informed independent decisions by providing the necessary facts and clarifying the alternatives and anticipated consequences; refer clients to other competent professionals when they are unable to support the clients; maintain as confidential any information received from clients, unless released by the client; and avoid exploiting clients for personal advantage, profit, or interest.[68]

Because both board certification and membership in the NSGC are voluntary, professional organizations cannot require or ensure that all persons holding themselves out as genetic counselors are appropriately trained.[69] Some commentators argue that

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[61] American Board of Genetic Counseling, "Certification Examination Program," website: *http://www.faseb.org/genetics/abgc/99-03.htm*, visited May 3, 1999; see note 29, above, on genetic specialists and the ABMG.

[62] American Board of Genetic Counseling, "Certification Examination Program," websites: *http://www.faseb.org/genetics/abgc/99-03.htm*; *http://www.faseb.org/genetics/abgc/99-06.htm*, visited May 3, 1999.

[63] Until recently, individuals who had practiced genetic counseling without having studied in programs certified by the ABGC were eligible to sit for the boards. Currently, only persons who have received master's degrees in genetic counseling are eligible to take the boards.

[64] American Board of Genetic Counseling, "Certification Examination Program," website: *http://www.faseb.org/genetics/abgc/99-04.htm*, visited May 3, 1999.

[65] E-mail correspondence with S. Robinson, M.S., ABMG/ABGC Administrator, American Board of Genetic Counseling, Bethesda, MD, December 22, 1999. Of the 1,410 genetic counselors, 631 were board-certified by the ABMG and 779 were board-certified by the ABGC. This total includes the most recently certified diplomates who took the board exam in June 1999. The board exams are held every three years.

[66] National Society of Genetic Counselors, "Code of Ethics," website: *http://www.nsgc.org/Taking_a_Stand.html*, visited July 2, 1999.

[67] Ibid.

[68] Ibid.

[69] Since no state requires licensure, certification, or registration of genetic counselors and board certification by the ABGC is voluntary, there is no accurate statistic on the number of persons who hold themselves out

individuals who perform genetic counseling functions without having received appropriate training sometimes misinform their patients.[70] Even among certified genetic counselors, recent surveys show that the issues and information included in counseling sessions varied widely.[71] Some commentators have called for an assessment of the process and outcomes of current genetic counseling practices and the establishment of guidelines for quality management in genetic counseling, especially as new genetic technologies are introduced into genetics services and primary care.[72]

## State Licensure or Certification of Genetic Counselors

### *State Licensure and Certification Generally*

Licensing laws govern entry into the licensed professions, disciplinary actions against licensed professionals, and the delivery of health care services by unlicensed persons.[73] In general, licensure restricts both practice of the profession and the use of the

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as genetic counselors or provide genetic counseling services as their primary profession or occupation. In a fall 1998 article, one commentator stated that there are 1,383 genetic counselors throughout the nation. C. Dunne and C. Warren, "Lethal Autonomy: The Malfunction of the Informed Consent Mechanism within the Context of Prenatal Diagnosis of Genetic Variants," *Issues in Law and Medicine* 14 (1998): 165, 190.

[70] Randi Zinberg, M.S., Genetic Counselor, Department of Human Genetics, Mount Sinai School of Medicine of the New York University, New York, NY, presentation to the New York State Task Force on Life and the Law, May 26, 1999.

[71] See B. B. Biesecker and T. M. Marteau, "The Future of Genetic Counseling: An International Perspective," *Nature Genetics* 22 (1999): 133, 134; R. Laux and M. Kershner, "Developing Prenatal Practice Guidelines," *Perspectives in Genetic Counseling* 21, no. 2 (1999): 13; Veach, "Client Perceptions," 193 (studies reported less satisfaction in three areas: the content of the information learned in counseling, feeling reassured, and receiving appropriate treatment); Dunne and Warren, "Lethal Autonomy," 186–189 (concluding that "individuals are receiving one-sided information during their prenatal consultations that lead to eugenic decisions"); E. T. Matloff, "Practice Variability in Prenatal Genetic Counseling," *Journal of Genetic Counseling* 3, no. 3 (1994): 215; see also D. Tilley and K. Ormond, "Abstracts from the Seventeenth Annual Education Conference of the National Society of Genetic Counselors (Denver, Colorado, October 1998)," *Journal of Genetic Counseling* 7 (1998): 445, 500–501 (abstract: D. C. Wertz, "'Can't Get No (Dis)satisfaction' Revisited: Providers' Reports of Satisfaction with Counseling Sessions").

[72] See Biesecker and Marteau, "The Future of Genetic Counseling," 134; Laux and Kershner, "Developing Prenatal Practice Guidelines," 13; M. Berkenstadt et al., "Perceived Personal Control (PPC): A New Concept in Measuring Outcome of Genetic Counseling," *American Journal of Medical Genetics* 82 (1999): 53 (study used a Perceived Personal Control scale to assess the psychological process and outcomes of genetic counseling); Veach, "Client Perceptions," 192, 214–215 (need for more studies on client perceptions of their genetic counseling experiences); K. Marymee et al., "Development of the Critical Elements of Genetic Evaluation and Genetic Counseling for Genetic Professionals and Perinatologists and Perinatologists in Washington State," *Journal of Genetic Counseling* 7, no. 2 (1998): 133; D. H. Lea, "Emerging Quality Improvement Measures in Genetic Counseling," *Journal of Genetic Counseling* 5, no. 3 (1996): 123.

[73] B. R. Furrow et al., *Health Law* (St. Paul, MN: West, 1995), § 3–1.

title of that profession to licensed individuals.[74] For example, in New York, only licensed physicians may practice medicine or use the title "physician."[75] Under New York law, the Board of Regents supervises and the Education Department regulates state licensing of professionals, including health care professionals.[76]

Other regulatory mechanisms, such as certification or registration, restrict the use of a particular title to individuals meeting specified requirements but do not restrict practice of that profession.[77] For example, in New York, only certified individuals may use the title "certified dietician" or "certified nutritionist,"[78] but noncertified persons may provide the services of a dietician or nutritionist as long as they do not use these titles. In general, state certification or registration of a profession would be less costly than licensure because it would not require the creation of a special state board for that profession.

***Current New York Practice***

In 1995, there were approximately 150 genetic counselors employed in New York State, and there were 96 genetic counselors with New York State addresses who were board-certified.[79] According to one source, "one-quarter to one-third of all individuals employed in New York State who call themselves genetic counselors are not board-certified."[80]

There is no law or regulation in New York State that regulates employment practices in genetic counseling or requires individuals performing genetic counseling to have specific training or to qualify for or take a certifying examination. Thus, without

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[74] Section 6503 of the Education Law provides that admission to the practice of a profession "(1) entitles the licensee to practice the profession as defined in the article for the particular profession, (2) entitles the individual licensee to use the professional title as provided in the article for the particular profession, and (3) subjects the licensee to the procedures and penalties for professional misconduct as prescribed in this article." N.Y. Educ. Law § 6503 (McKinney 1999).

[75] N.Y. Educ. Law § 6522 (McKinney 1999).

[76] N.Y. Educ. Law §§ 6506, 6507 (McKinney 1999).

[77] This "statutory" certification is distinct from the certification conferred by professional associations, although state statutes often rely on professional certification in their regulation of the occupation. E. Graddy, "Interest Groups or the Public Interest — Why Do We Regulate Health Occupations?" *Journal of Health Politics, Policy and Law* 16, no. 1 (1991): 25, 26 n.2.

[78] N.Y. Educ. Law § 8002 (McKinney 1999).

[79] Memorandum by Elsa Reich, M.S., C.G.C., to Hon. Edward Sullivan, Chairman, New York State Assembly Committee on Higher Education, December 11, 1996. According to Ms. Reich, the "150 genetic counselors" include (i) both those who are board-certified or board-eligible and those who are not board-certified or board-eligible and (ii) both those who live in New York and those who live outside New York. The "96 genetic counselors with New York State addresses" may include board-certified genetic counselors who (i) live and work in New York, (ii) live in New York but work outside New York, or (iii) live outside New York but work in New York. However, since there are very few genetic counselors who work in New York but live outside New York, or vice versa, Ms. Reich estimated that approximately one-third of genetic counselors working in New York State in 1995 were not board-certified. Telephone conversation with Elsa Reich, May 11, 1999.

[80] Ibid.

any government oversight, there is an unknown number of untrained individuals acting as genetic counselors. Furthermore, there are no criteria by which consumers can determine whether a genetic counselor is adequately trained and/or competent to provide genetic counseling.

### *Previous Efforts to License Genetic Counselors in New York State*

In New York State, beginning in about 1990, a group of genetic counselors lobbied the New York State Education Department and later the state legislature to license genetic counselors. Despite their efforts, the final version of a proposed bill[81] to license genetic counselors failed in 1997 for a number of reasons, including concerns about the high cost of licensing a very small group of genetic counselors and opposition from the medical community and the insurance industry.[82]

### *Policy Issues Related to Licensure or Certification*

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[81] A.B. 1189, 221st Leg. (N.Y. 1997). The proposed bill would have limited the practice of genetic counseling to licensed genetic counselors, medical geneticists, and clinical geneticists. Only individuals licensed under the law would be permitted to use the title "licensed genetic counselor." Other professionally licensed individuals, such as physicians, would be permitted to perform genetic counseling as long as it was within the exercise of their licensed profession. However, professionals without a genetic counselor license would have been prohibited from performing certain tasks. Under the proposed legislation, a licensed genetic counselor would have been required to have completed the academic preparation and supervised clinical work and examinations required for certification, be certified in genetic counseling by the ABGC or in Ph.D. medical genetics by the ABMG, pay a registration or license fee of $100, and swear that he or she is at least 21 years of age and of good moral character. Provisional licenses also would have been available for candidates who had been granted "board-eligible" status by the ABGC. A licensed genetic counselor would have been required to satisfy any continuing education requirements promulgated by the Commissioner of Health and renew the license every two years.

The bill also provided for the creation of a genetics advisory council to advise the Commissioner of Health "with regard to the professional conduct of licensed genetic counselors and to the implications of the uses of new genetic tests on individual liberties, civil rights and social justice." The duties of the advisory council would have included, among other things, identifying genetic tests that predict with high probability seriously life-threatening diseases or severe disability and advising the Commissioner in each case whether to require genetic counseling as part of informed consent and identifying criteria by which primary care and other physicians should recognize the need to refer patients to licensed genetic counselors. Licensed genetic counselors would have been subject to the disciplinary rules and procedures of the state Board for Professional Medical Conduct.

According to a genetic counselor who was involved with the licensing initiative, earlier versions of the proposed bill contained a provision that certain genetic tests would require genetic counseling, which was later deleted and changed in favor of a provision authorizing the advisory council to determine if and when counseling should be required. Meeting of genetic counselors with Task Force staff on May 5, 1999. Nevertheless, the proposed bill A.1189 would have authorized the commissioner to "promulgate rules designating counseling by licensed genetic counselors . . . as a necessary component of informed consent to undergo certain tests pursuant to the advice of the genetics advisory council."

[82] Meeting of genetic counselors with Task Force staff on May 5, 1999.

In addition to New York, there have been efforts to license genetic counselors in other states.[83] Most genetic counselors favor the licensing of their profession.[84] Proponents of state licensure of genetic counselors make the following arguments:[85]

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[83] See, e.g., A.B. 1488, 209th Leg. (N.J. 2000); L.B. 736, 96th Leg., 1st Reg. Sess. (Neb. 1999).

New Jersey's proposed bill provides that no person shall practice genetic counseling or call himself or herself a genetic counselor without a genetic counselor license issued by the State Board of Medical Examiners. To obtain a license, an applicant must have a current and valid certificate as "certified genetic counselor" from the ABMG or ABGC and pay a licensing fee. Provisional licenses could be issued to applicants who are granted board-eligible status by the ABGC. As with the New York bill, the New Jersey bill's licensing requirements would not apply to persons licensed to practice medicine and surgery when acting within the scope of their profession and consistent with their training, as long as they do not call themselves licensed genetic counselors. In addition, the New Jersey bill would not apply to students in accredited genetic counseling programs, genetic assistants performing limited counseling under the supervision of a medical geneticist or licensed genetic counselor, and licensed registered nurses when acting within the scope of their profession. Also, like the New York bill, the New Jersey bill provides for the creation of a genetic counseling advisory committee and would require license renewal every two years. However, unlike the New York bill, New Jersey's bill would require that genetic counselors maintain their certification by the ABMG or ABGC and satisfy any continuing education requirements of the ABGC in order to renew their license. The New Jersey bill also contains provisions relating to the nondisclosure of confidential information, unlike the New York bill, which does not address this issue. See also Chapter 9, pages 257–262.

Nebraska's bill provides that anyone "providing clinical diagnostic and genetic counseling services shall have appropriate state licensure or be certified by" the ABMG or the ABGC.

While California does not have a statute requiring licensure of genetic counselors, legislation in California directs the state Department of Health Services to make recommendations for licensing criteria and standards to the state legislature by January 1, 2000. Cal. Hereditary Disorders Act, Cal. Health & Safety Code § 124980(b) (West 1998). In addition, California has a statute providing that individuals with a master's degree in genetic counseling who are board-eligible or board-certified by the ABMG and ABGC may become "sickle cell counselors" without undergoing an otherwise required training program. Cal. Admin. Code tit. 17, § 6500 (t) (West 1999).

Washington recognizes the practice of genetic counseling in its statutes governing the Department of Health, which define "qualified genetic counselor" as an individual eligible for certification or certified, as defined in the ABGC's 1984 Bulletin of Information, as a genetic counselor, clinical geneticist, Ph.D. medical geneticist, clinical cytogeneticist, or clinical biochemical geneticist. Wash. Admin. Code § 246-680-010 (9) (1998). The Washington regulations allow genetic counselors to order genetic tests.

In Colorado, genetic counselors who offer prenatal screening may have some statutory protection from civil suits arising out of their services. The Colorado Health Care Availability Act precludes recovery "for any damage or injury arising from genetic counseling and screening and prenatal care, . . . where such damage or injury was the result of genetic disease or disorder or other natural causes, unless the claimant can establish by a preponderance of the evidence that the damage or injury could have been prevented or avoided by ordinary standard of care of the physician or other health care professional or health care institution." Colo. Rev. Stat. Ann. § 13-64-502 (West 1999). It is not clear whether "other health care professional" includes genetic counselors.

[84] Randi Zinberg, M.S., Genetic Counselor, Department of Human Genetics, Mount Sinai School of Medicine of the New York University, New York, NY, presentation to the New York State Task Force on Life and the Law, May 26, 1999.

[85] S. Schmerler, "Licensure: Two Sides of the Coin — On the 'Head' Side," *Perspectives in Genetic Counseling*, National Society of Genetic Counselors 19, no. 4 (1997/1998): 1, 1, 13; Meeting of genetic counselors with Task Force staff on May 5, 1999. In a 1985 survey of genetic counselors in California, half of the respondents expressed some interest in licensure. Scott et al., "Genetic Counselor Training," 197.

- Lack of statutory requirements for the practice of genetic counseling allows unqualified and untrained individuals to enter the field
- Licensure could promote a higher level of proficiency and knowledge among counselors by requiring continuing education and recertification
- Licensure would help genetic counselors obtain reimbursement, thereby allowing genetic counseling to become a viable practice[86] — which is particularly important given the growth of genetic testing and the lack of knowledge about genetic testing among physicians[87]
- Licensing would elevate the stature of the profession, which would encourage more people to enter the field
- A state licensing board could provide the public with information about genetic counseling and genetic counselors and a mechanism for consumer complaints

Commentators who oppose licensure argue that the cost of licensing a very small number of genetic counselors is too high. Moreover, they maintain that these costs would raise the cost of providing genetic counseling services, thereby limiting access to such services.[88]

### Scope of Practice

#### *Independent Practice*

Most genetic counselors practice as an integral part of a genetics services delivery team that includes medical geneticists, Ph.D. geneticists, primary care physicians, and specialty-trained physicians (e.g., oncologists, obstetrician-gynecologists, and neonatologists) in a variety of areas, including obstetrics, gynecology, pediatrics, and

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[86] B. A. Bernhardt and R. E. Pyeritz, "The Economics of Clinical Genetics Services. III. Cognitive Genetics Services Are Not Self-Supporting," *American Journal of Human Genetics* 44 (1989): 288, 291–293.

[87] Some genetic counselors report that they have worked with many physicians who do not have adequate knowledge about genetics or genetic testing. Meeting of genetic counselors with Task Force staff on May 5, 1999. At a Task Force meeting in April 1998, Dr. Gail Geller, Sc.D., Genetics and Public Policy Studies, Johns Hopkins University School of Medicine, Baltimore, MD and Katherine Schneider, M.P.H., Genetic Counselor, Dana Farber Cancer Institute, Boston, MA, expressed concerns about the ability of primary care physicians to recommend and adequately counsel for testing. Dr. Geller presented results from a questionnaire-based survey she performed to assess differences in attitudes about genetic cancer susceptibility testing issues. Some of the survey results included the following: 34 percent of physicians would not discuss concerns about insurance discrimination with persons considering cancer susceptibility testing, 16 percent of physicians did not think that informed consent for testing was important, and a minority of physicians could correctly calculate a positive predictive value. See also pages 362–364, this chapter.

[88] W. A. Faucett, "Licensure: Two Sides of the Coin — On the 'Tail' Side," *Perspectives in Genetic Counseling*, National Society of Genetic Counselors 19, no. 4 (1997/1998): 1, 1, 13; Meeting of genetic counselors with Task Force staff on May 5, 1999.

internal medicine.[89] According to a 1998 survey by the NSGC, only 1 percent of genetic counselors work in private practices; nearly all of the genetic counselors surveyed work in institutional settings.[90] Many genetic counselors believe that the lack of professional licensure and their inability to receive reimbursement for services are the reasons they are unable to practice independently.[91] While many genetic counselors would support the ability to practice independently, a minority is concerned that inexperienced genetic counselors — recent graduates or newly certified counselors, for example — with an independent practice may do more harm than good because they would not have adequate training from working in clinical settings. Other commentators go even further to argue that genetic counselors should always practice under the supervision of physicians.[92]

### *Ordering Genetic Testing*

Under current New York law, genetic counselors can order genetic testing for their patients only through persons who are authorized by law to do so, such as licensed physicians and nurse practitioners.[93] At least one other state, however, allows genetic counselors to order genetic tests.[94] Many genetic counselors believe that they should be able to order genetic tests in certain circumstances — for example, ordering a breast cancer susceptibility gene (BRCA) test for a patient with significant family history of breast cancer.[95] Others, however, have expressed concern that the ability to order genetic testing would further blur the distinction between practicing medicine and genetic counseling.[96]

### *Meeting the Increased Demand for Genetic Counseling*

Some commentators predict that as more genetic tests and therapies become more available, there will be too few genetic counselors to meet demands for testing and

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[89] Blatt, "Medical Genetic Services," website: *http://www.geneletter.org*; J. V. Dailey, M. A. Pagnotto, and S. Fontana-Bitton, "Role of the Genetic Counselor: An Overview," *Journal of Perinatal and Neonatal Nursing* 9, no. 3 (1995): 32, 34.

[90] National Society of Genetic Counselors website: *http://www.nsgc.org/Careers.html*, visited May 3, 1999; see also Tilley and Ormond, "Abstracts from the Seventeenth Annual Education Conference," 508 (abstract: B. Lerner, A. Warner, and D. Eakman, "Expanding the Opportunities for Genetic Counselors in Private Practice").

[91] Meeting of genetic counselors with Task Force staff on May 5, 1999. See also Bernhardt and Pyeritz, "The Economics of Clinical Genetics Services. III," 291–293.

[92] Meeting of genetic counselors with Task Force staff on May 5, 1999.

[93] 10 N.Y.C.R.R. § 58-1.7(b) (1999) ("a clinical laboratory shall examine specimens only at the request of licensed physicians or other persons authorized by law to use the findings of laboratory examinations in their practice or the performance of their official duties. . . . (1) Other persons authorized by law to request the examination of specimens shall include but not be limited to: (i) dentists and podiatrists . . . (ii) chiropractors . . . (iii) physician's assistants and certified nurse-midwives, provided such examination is authorized by the supervising physician; (iv) nurse practitioners . . . (v) police officers, provided such examination is incident to arrest charges for alcohol or drug impairment; and (vi) judges ordering paternity tests under the Family Court Act").

[94] That state is Washington. Meeting of genetic counselors with Task Force staff on May 5, 1999.

[95] Ibid.

[96] Ibid.

services.[97] A 1990 New York State survey of fifty-seven genetic service centers found a shortage of genetic counselors.[98] At the time of the survey, those questioned estimated that the workload warranted 50 percent more genetic counselors than were available.

## Primary Care Physicians and Nongenetics Physician Specialists

### Competence in Genetics

Most commentators predict that as advances in genetics continue to develop, there will be too few genetics professionals to meet the growing demands for genetics services, and, therefore, primary care physicians[99] will need to offer some genetics services, including genetic testing.[100] Indeed, some studies show that primary care physicians are already providing some genetics services in response to increasing demands from their patients.[101] However, many practicing physicians have no medical school training in genetics and do not have the knowledge or clinical training to integrate genetics into

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[97] See "Genetics Counselors Will Have Expanded Role," *Medical Ethics Advisor* 17, no. 1 (2000): 4, 6; Collins, "Preparing Health Professionals," 1285; Wertz, "Society and the Not-So-New Genetics," 343; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 211.

[98] Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 211; R. Zinberg and K. Greendale, "Do We Have a Shortage of Genetic Counselors in New York State?" *The Newsletter of the Genetics Network of the Empire State* 3 (1991): 1.

[99] Primary care practitioners include family practitioners, internists, and obstetrician-gynecologists.

[100] See F. S. Collins, "Genetics: Not Just in There Somewhere, But at the Very Center of Medicine," *Genetics in Medicine* 1 (1998): 3; National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing in the United States*, ed. N. A. Holtzman and M. S. Watson (Washington, D.C.: National Institutes of Health, 1997), 62; Collins, "Preparing Health Professionals," 1285–1286 ("According to surveys, however, most health professionals are not prepared to integrate genetics into clinical practice. . . . Surveys also show that many health professionals have insufficient knowledge of available genetic resources."); G. Geller et al., "Consensus Statement — Genetic Testing for Susceptibility to Adult-Onset Cancer," *Journal of the American Medical Association* 277 (1997): 1467, 1468 ("Obstacles to medical professionals' assisting participants in understanding genetic information include their own lack of genetics knowledge, their inadequacy at communicating probabilistic information, their cynicism about the validity of the informed consent process, and their tendency to be directive."); Wertz, "Society and the Not-So-New Genetics," 306–307 ("Given the small number of geneticists . . . most genetic information, and probably most genetic tests, will be provided to patients by their primary care physicians rather than by genetic specialists. Although inevitable, this is worrisome in view of the gaps in knowledge . . . among the primary care physicians . . . some gave incorrect answers to questions of considerable importance to patients."); "Optimizing Genetic Services in a Social, Ethical, and Policy Context: Suggestions from Consumers and Providers in the New England Regional Genetics Group (NERGG)," *The Genetic Resource* 10, no. 2 (1996): 14 ("consumers reported difficulty in convincing either primary caregivers or specialists to make appropriate referrals to specialists"); Bernhardt and Pyeritz, "Organization and Delivery," 3; President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Screening and Counseling for Genetic Conditions*, 35.

[101] Touchette et al., *Toward the 21st Century*, 26.

primary care services.[102] A number of studies reveal that the lack of knowledge and training in genetics has led to errors and problems, such as the inability to keep pace with genomic science and its clinical applications, failure to recognize patients who may benefit from genetics services, difficulty in interpreting probabilistic information, low tolerance for uncertainty, and lack of skills for performance of nondirective genetic counseling. For example:

- One study of primary care physicians' utilization and perceptions of genetics services found that physicians frequently failed to seek appropriate genetics consultations for disorders such as deafness, polycystic kidney disease, or congenital heart disease. The most common reason for not seeking consultations was the perception that they had no benefit to the patient. The study also found that physicians view the genetics specialist as someone who only treats "rare and esoteric" disorders and that even when uncertain or wrong about a patient's genetics risks, physicians usually counseled a patient themselves rather than referring to a specialist.[103]

- In one study of genetic testing of individuals at risk for familial colon cancer, only 19 percent of patients received genetic counseling, and nearly one-third of physicians misinterpreted negative test results.[104]

- A survey of the obstetrics-gynecology community found that physicians are not prepared to comply with an April 1997 National Institutes of Health Consensus Statement to offer prenatal carrier screening for cystic fibrosis.[105] The total correct response to a questionnaire covering testing-related issues was 66 percent, with younger and less experienced physicians generally showing higher scores than older physicians.[106]

- A survey of practitioners who were among the first to inquire about and use the BRCA1/2 genetic tests outside of a research protocol found that many practitioners have an interest in BRCA1/2 testing despite policy statements that discourage its use

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[102] Collins, "Preparing Health Professionals," 1286. One national survey of 329 health professionals who provide services to people with genetic disorders in university-affiliated programs across the country found that almost 70 percent reported having no course work in human genetics. "HuGEM to Educate Health Professionals in Genetics," *Human Genome News* 9, no. 1–2 (1998): 12.

[103] S. J. Hayflick et al., "Primary Care Physicians' Utilization and Perceptions of Genetics Services," *Genetics in Medicine* 1 (1998): 13, 17.

[104] F. M. Giardiello et al., "The Use and Interpretation of Commercial APC Genetic Testing for Familial Adenomatous Polyposis," *New England Journal of Medicine* 336 (1997): 823; see also Chapter 8, page 222.

[105] For a discussion of the statement, see Chapter 5, page 117.

[106] J. A. Kuller, R. Baughan, and C. Biolosi, "Cystic Fibrosis and the National Institutes of Health Consensus Statement: Are Obstetrician-Gynecologists Ready to Comply?" *Obstetrics and Gynecology* 93 (1999): 581. See also W. W. Grody et al., "Diversity of Cystic Fibrosis Mutation-Screening Practices," *American Journal of Human Genetics* 62 (1998): 1252 (illustrating the increasing complexity of cystic fibrosis screening mutation panels); M. T. Mennuti, E. Thomson, and N. Press, "Screening for Cystic Fibrosis Carrier State," *Obstetrics and Gynecology* 93 (1999): 456, 460 ("Primary care provider education is necessary before implementation of widespread genetic testing for cystic fibrosis.").

outside of research protocols and that 28 percent of physicians who ordered a BRCA1/2 test reported having no access to a genetic counselor.[107]

- A survey of 175 obstetrical visits showed that only 40 percent of nongeneticist providers offered patients a referral for genetic counseling and that patients received inaccurate information about prenatal genetic testing.[108]

- In some studies, physicians scored poorly on genetic quizzes.[109]

Other data indicate similar inadequacies of genetics knowledge among nursing and other allied health professionals. In response, the National Human Genome Research Institute (NHGRI) program for ethical, social, and legal implications (ELSI) has expressed concern about the ability of health care providers, as well as the general public, to keep up with information generated by the Human Genome Project and its impact on medical practice. It declared professional and public education to be one of four issues assigned high priority for support.[110]

*Promoting Genetics Competence in Physician Training*

### *Medical School and Postgraduate Education*

Most commentators agree that education in genetics should take place in medical school and intern training.[111] Medical schools have begun including human genetics in their curriculum within the last two decades, but the current genetics curricula among the 126 U.S. medical schools vary widely.[112] To help schools develop curricula, the ASHG produced a list of objectives for medical school core curriculum in genetics and the skills and attitudes that schools should promote.[113] Following medical school and internship

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[107] M. K. Cho et al., "Commercialization of BRCA1/2 Testing: Practitioner Awareness and Use of a Genetic Test," *American Journal of Medical Genetics* 83 (1999): 157.

[108] D. C. Wertz, "Prenatal Genetic Testing: What Do Obstetrical Providers Discuss with Patients?" *GeneLetter* (January 1997), website: *http://www.geneletter.com*, visited July 18, 2000.

[109] See, e.g., N. A. Holtzman, "Bringing Genetic Tests into the Clinic," *Hospital Practice*, January 19, 1999, 107, 125; L. Wilkins-Haug et al., "Genetics in Obstetricians' Offices: A Survey Study," *Obstetrics and Gynecology* 93 (1999): 642; Kuller, Baughan, and Biolosi, "Cystic Fibrosis," 581. See Chapter 4, page 91, for discussion on the misperceptions about medical genetic testing.

[110] See National Human Genome Research Institute website: *http://www.nhgri.nih.gov/About_NHGRI/Der/Elsi/high_priority.html*, visited January 27, 2000; see also Chapter 11, page 318.

[111] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 65; Institute of Medicine Committee on Assessing Genetic Risks, *Assessing Genetic Risks*, 216–220.

[112] M. Mitka, "AMA to Help Doctors Get Most from Genetic Breakthroughs," *American Medical Association News*, September 22/29, 1997, 4; NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 65. The NIH-DOE Task Force on Genetic Testing report cites a 1995 survey showing that only sixty-eight medical schools required genetics courses in their curricula.

[113] American Society of Human Genetics Information and Education Committee, "Report from the ASHG Information and Education Committee: Medical School Core Curriculum in Genetics," *American Journal of Human Genetics* 56 (1995): 535. More recently, the Association of Professors of Human or Medical Genetics developed a list of clinical objectives in medical genetics intended to complement the ASHG core

training, integration of medical genetics into specialty training varies by specialty areas and individual programs.

More recently, the NHGRI has established an Interagency Agreement with the Health Resources and Services Administration to provide faculty development in genetic medicine for Family Practice, Pediatric, and Internal Medicine physician faculty who teach primary care medicine to medical students and/or residents in ambulatory, community-based settings. This project aims to prepare academic faculty and their community colleagues with the knowledge, skills, and attitudes essential to teaching and integrating genetic medicine into primary care.[114]

### *Licensure of Physicians*

New York law requires licensure for the practice of medicine and use of the title "physician"[115] and establishes a state board for medicine to oversee licensure.[116] Licensure requirements include a doctor of medicine or osteopathy degree, relevant postgraduate experience, and passage of a national medical board examination. In recent years, the National Board of Medical Examiners has begun to reevaluate how effectively the licensure examinations for medical students assess genetics knowledge.[117] The National Institutes of Health-U.S. Department of Energy Working Group on Ethical, Legal, and Social Implications of Human Genome Research Task Force on Genetic Testing (NIH-DOE Task Force on Genetic Testing) (1997) concluded that the likelihood that genetics will be covered in medical school and postgraduate training will improve if "correctly answering a proportion of the genetics questions is needed to attain a passing score."[118]

## Promoting Genetics Competence by Continuing Medical Education

### *Continuing Medical Education in Genetics*

Continuing medical education (CME), through formal courses or less formal approaches, such as community-based outreach activities, enables physicians to keep up-to-date in rapidly evolving areas of clinical medicine. Given that few primary care practitioners have had medical school training in genetics, CME has become the primary mechanism through which physicians acquire and update their knowledge of genetics. A 1999 survey of ninety-six medical specialty societies' current and planned CME activities in genetics reveals that 64 percent of respondents currently have no CME genetics modules, but

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curriculum guidelines. Association of Professors of Human Genetics, "Clinical Objectives in Medical Genetics for Undergraduate Medical Students," *Genetics in Medicine* 1 (1998): 54.

[114] National Human Genome Research Institute website: *http://www.nhgri.nih.gov/About_NHGRI/Der/Elsi/high_priority.html*, visited January 27, 2000

[115] N.Y. Education Law § 6522 (McKinney 1999).

[116] Ibid., §6523.

[117] See NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 66.

[118] Ibid., xxi.

that 67 percent are interested in their development.[119] A survey of specialty societies' annual meetings reveals that only 37 percent have programs focused on clinical genetics issues of that specialty. The study reported that the majority of medical societies recognize the need for collaborative educational efforts to integrate genetics into practice.

In recent years, there have been many initiatives for genetics-based CME for primary care physicians and other allied health professionals. In addition to formal didactic sessions, for example at annual specialty meetings, many other approaches are being tried, including development of educational Internet sites and community-based grassroots approaches. For example, a primary care provider genetics education model and curriculum entitled "Genetics & Your Practice" was developed in a collaborative project of the Washington State Department of Health, the Western Washington Chapter of the March of Dimes Birth Defects Foundation, and genetic service providers throughout Washington and funded by a Maternal and Child Health Bureau grant.[120] The project has been expanded to seventeen March of Dimes pilot sites across the country, including the Greater New York Chapter of the March of Dimes in New York City.[121]

One New York geneticist who is actively involved in genetics CME initiatives opines that professionals who develop CME formats need to consider when and how busy primary care physicians will determine that genetics is relevant to their practice, rather than planning broad one-shot courses that are often poorly attended.[122] For example, an AMA conference for genetics for primary care physicians in 1998 had difficulty enrolling

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[119] S. V. Spilson, "Defining the Current Status of Medical Genetics in Continued Professional Development," The Second National Conference on Genetics and Disease Prevention: Integrating Genetics into Public Health Policy, Research, and Practice, Baltimore, MD, December 6–8, 1999.

[120] Washington State Genetics Documents website: *http://mchneighborhood.ichp.edu/wagenetics*, visited May 24, 1999. The curriculum of "Genetics & Your Practice" attempts to help physicians and other health care providers in four ways: (a) raising awareness of genetic health care issues, (b) assessing and identifying individuals at risk for genetic diseases, (c) diagnosing and treating affected or at-risk individuals, and (d) reducing risk status and/or improving outcomes. The education model of "Genetics & Your Practice" is primarily didactic and uses different types of audiovisual aids. Ibid. at *http://mchneighborhood.ichp.edu/wagenetics/906317753.html*.

[121] For more information, contact Director of Program Services, Greater New York Chapter, March of Dimes, 233 Park Avenue South, 3rd Floor, New York, New York 10003, tel. (212) 353-8499, fax (212) 254-3518, e-mail: *nandino@modimes.org*.

[122] Telephone interview with Dr. Jessica Davis, May 13, 1999. Dr. Davis cited a study on the effectiveness of CME that concluded that widely used CME strategies such as conferences have little impact on improving professional practice and that more effective methods such as systematic practice-based interventions and outreach visits are seldom used by CME providers. See D. A. Davis et al., "Changing Physician Performance — A Systematic Review of the Effect of Continuing Medical Education Strategies," *Journal of the American Medical Association* 274 (1995): 700.

participants, even when registration fees were suspended.[123] One specialty area that is successfully integrating genetics into its mainstream practice is oncology, prompted to do so by development of and public attention to cancer genetic susceptibility testing.[124]

### *Clinical Guidelines for Genetics Medicine*

Clinical guidelines play an important role in physician education and practice. Timely and accurate clinical guidelines by genetics and other professional societies, which consider the scientific, medical, and ethical issues of genetic testing, can guide primary care as well as specialty practitioners. Some commentators suggest that clinical guidelines in genetics are needed at the institutional, regional, state, and federal levels. Some have noted that although millions of federal dollars are dedicated to the Human Genome Project and its ELSI program, "funds for training and service delivery, including clinical guideline and other quality improvement efforts, are sparse."[125] In recent years, the New York State Department of Health funded the ACMG to produce clinical guidelines for BRCA testing and for recognition of congenital malformations.[126]

## *The National Coalition for Health Professional Education in Genetics*

In 1996, the American Nurses Association (ANA), the AMA, and the NHGRI created the National Coalition for Health Professional Education in Genetics (NCHPEG) as part of a national effort to promote health professional education and access to information about advances in human genetics.[127] NCHPEG members are an interdisciplinary group of leaders from diverse health professional organizations, consumer and voluntary groups, government agencies, private industry, managed care organizations, and genetics professional societies. NCHPEG's goals include: (1) development of a comprehensive, web-based genetics information center; (2) development of a core curriculum in genetics to serve as a template for modification according to health professional discipline; and (3) integration into continuing education programs, licensure, and certification programs.[128] The web-based genetics information center provides both clinicians and the public with information sources about the science

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[123] Telephone interview with Dr. Priscilla Short, Director, Office of Biomedical Science and Clinical Research, American Medical Association, Washington, D.C., May 24, 1999. The not-very-well attended AMA genetics conference was held on March 13–15, 1998, in New Orleans, Louisiana.

[124] D. M. Livingston, "Genetics Is Coming to Oncology," *Journal of the American Medical Association* 277 (1997): 1476, 1477. See also NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 69, and the American Society of Clinical Oncology website: *http://www.asco.org/prof/ps/html/m_gencur.htm*, visited May 11, 1999.

[125] Jessica Davis, M.D., and Karen Greendale, M.A., C.G.C., "Quality Assurance for Genetic Service Delivery," New York State University of Albany School of Public Health, November 10, 1998.

[126] The guidelines, entitled *Genetic Susceptibility to Breast and Ovarian Cancer: Counseling and Testing* and *The Evaluation of the Newborn with Single and Multiple Congenital Anomalies*, were released in 1999. See also Chapter 11, pages 333 and 337.

[127] National Coalition for Health Professional Education in Genetics website: *http://www.nchpeg.org*, visited January 25, 2000.

[128] Ibid.

of genetics and genetic disorders as well as ethical and practice issues raised by genetic testing. It also provides referral lists of genetic counselors, specialists, and testing laboratories.[129]

***Approaches to Promote Continuing Medical Genetics Education***

## *Specialty Board Certification*

Physicians may obtain board certification in relevant specialty areas through the appropriate professional specialty boards. Specialty boards evaluate candidates who voluntarily appear for examination and certify as diplomates those who qualify. The purpose of certification is to assure the public that a certified medical specialist has successfully completed an approved educational program and an evaluation designed to assess knowledge, experience, and skills requisite to specialty care.[130] All specialty boards now require periodic recertification, generally every seven to ten years.[131]

Certification examinations vary in their assessment of genetics competencies. In 1997, the NIH-DOE Task Force on Genetic Testing concluded that for both licensure and specialty board exams, with some exceptions, questions involving genetics "are sparse and sometimes inappropriate."[132] They and others have suggested that those responsible for medical licensure and board examinations provide more emphasis on genetics and require a baseline score in genetics to pass the exam.[133] They have also called on the individual specialty boards to design their own curricula for continuing education in genetics.[134]

*State Licensing Boards with CME Requirements*

A majority of state medical licensing boards have CME requirements for recredentialing of licensed physicians.[135] New York requires licensed physicians to register with the state

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[129] National Coalition for Health Professional Education in Genetics website: *http://www.nchpeg.org*, visited January 27, 2000.

[130] American Board of Medical Specialties Public Education Program website: *http:// www.certifieddoctor.com*, visited May 13, 1999.

[131] American Board of Medical Specialties website: *http://www.abms.org*, visited May 13, 1999. Its mission is to improve the quality of medical care by assisting member boards in their efforts to develop and utilize professional and educational standards for the evaluation and certification of physician specialists. Telephone interview with American Board of Medical Specialties, general information, May 26,1999.

[132] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 66. Exceptions cited included the American Board of Obstetricians and Gynecologists and the Society of Perinatal Obstetricians.

[133] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, xxi; Collins, "Preparing Health Professionals," 1286.

[134] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 67.

[135] U.S. Medical Licensure Statistics and Requirements by State for 1998–1990, "Licensing Boards with CME Requirements" (table of state medical licensing boards with CME requirements for the fifty states, District of Columbia, Guam, Puerto Rico, and Virgin Islands). Thirty-five state medical boards have implemented CME requirements, ranging from twelve hours per year (Alabama) to as much as fifty hours per year (Guam, Hawaii, Idaho, Illinois, Kansas, Maine, Massachusetts, Michigan, New Hampshire, Ohio,

every two years.[136] However, unlike most other states, New York's only CME requirements for registration are that physician applicants attend a two-hour course in the identification and reporting of child abuse and coursework in infection control to prevent the transmission of HIV and hepatitis B infections in health care settings.[137] Some have suggested that states should consider a requirement for genetics CME as a condition of registration.[138] The Medical Society for the State of New York opposes making CME a mandatory condition for obtaining or maintaining medical licenses.[139]

*Medical Organization-Based Requirements for Genetics Education*

Managed care organizations and hospitals also can guide their member providers to ensure appropriate use of genetic testing and counseling services and appropriate referrals to specialists. For example, in 1999, Aetna U.S. Healthcare produced a series of guidelines to assist its practitioners in genetic testing and counseling decisions and processes in the context of women's health. Their guidelines for BRCA gene testing state that adequate counseling is "essential" and provide criteria to assess who is an appropriate candidate for counseling and testing.[140]

The NIH-DOE Task Force on Genetic Testing recommended that hospitals and managed care organizations, on advice from the relevant medical specialty departments, should require evidence of competence before permitting providers to offer or counsel for complex predictive genetic tests.[141] They also recommended periodic, systematic medical record review, with feedback to providers, to ensure appropriate services. The NIH-DOE Task Force on Genetic Testing did not favor requiring organizations to establish competency requirements. In a physician survey, a majority supported the idea that physicians should be required to undergo a brief certification in genetics before they could order susceptibility tests; about 19 percent agreed strongly, and approximately 25 percent disagreed strongly.[142]

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Oklahoma, Washington). The table shows that seventeen states have no CME requirements: Colorado, Connecticut, Indiana, Louisiana, Mississippi, Montana, New Jersey, New York, North Carolina, Oregon, Pennsylvania, South Carolina, South Dakota, Tennessee, Vermont, Virginia, and Wyoming.

[136] N.Y. Education Law § 6502(1) (McKinney 1999).

[137] New York State Education Department website: *http://www.nysed.gov/prof/med.htm*, visited May 13, 1999; U.S. Medical Licensure Statistics and Requirements by State for 1998–1990, "Licensing Boards with CME Requirements."

[138] Telephone interview with Dr. Priscilla Short, Director, Office of Biomedical Science and Clinical Research, American Medical Association, Washington, D.C., May 24, 1999.

[139] Medical Society for the State of New York website: *http://www.mssny.org/members_only/licensure.htm*, visited May 12, 1999.

[140] Telephone interview with Dr. Alan Bombard, Medical Director, West Region, Women's Health, Aetna U.S. Healthcare, San Ramon, CA, June 11, 1999.

[141] NIH-DOE Task Force on Genetic Testing, *Promoting Safe and Effective Genetic Testing*, 67–69.

[142] Ibid., 69.

## Nurses

While some graduate nursing programs have already incorporated genetics and genetic counseling into their programs, few practicing nurses are currently trained in genetics.[143] The single most important barrier preventing widespread dissemination of genetics knowledge is a lack of relevant and accessible sources of this knowledge for students, practicing nurses, and faculty. A 1993 survey of deans and chairs of master's-level nursing programs with an option in genetics indicated only 22 nurses graduated from six such academic programs between 1983 and 1994.[144]

### Genetic Nurse Specialists

Genetics nursing is a separate clinical specialty that focuses on providing nursing care to clients who have known genetic conditions and/or birth defects, who are at risk of developing them, or who have children with genetic conditions and/or birth defects.[145] Genetic nurse specialists are typically registered nurses (R.N.s) or masters'-level nurses with special training in human genetics.[146] In 1996, there were approximately 160 genetic nurse specialists in the United States.[147]

For predictive genetic testing, master's-prepared nurse specialists have a major role in identifying patients and families at risk for developing a disease with a genetic component.[148] The main nursing activities in genetics nursing practice are:[149]

- Helping with collecting, reporting, and recording genetic information, including a thorough family and reproductive history

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[143] Wertz, "Society and the Not-So-New Genetics," 305.

[144] R. B. Monsen and G. Anderson, "Continuing Education for Nurses That Incorporates Genetics," *Journal of Continuing Education in Nursing* 30, no. 1 (1999): 20, 22. In 1995, the NSGC identified five existing graduate nursing programs offering specialization in the field of genetics, of which one prepares its graduates to be board-eligible for the ABGC certification examination. The programs listed are: UCLA Neuropsychiatric Institute, Rush University College of Nursing, University of Iowa College of Nursing, University of Cincinnati College of Nursing and Health, and Eunice Kennedy Shriver UAP. Dailey, Pagnotto, and Fontana-Bitton, "Role of the Genetic Counselor," 33.

[145] International Society of Nurses in Genetics, Inc., and American Nurses Association, *Statement on the Scope and Standards of Genetics Clinical Nursing Practice* (Washington, D.C.: American Nurses Publishing, 1998), 2.

[146] GeneTests™, "Genetic Counseling and Testing, Clinical Genetics Professionals," website: *http:// www.genetests.org*, visited September 30, 1999.

[147] Monsen and Anderson, "Continuing Education for Nurses," 21.

[148] I. Forsman, "Evolution of the Nursing Role in Genetics," *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 23 (1994): 481, 484.

[149] Lea, Jenkins, and Francomano, *Genetics in Clinical Practice,* 72–108.

- Offering genetic information and resources to patients and families
- Supporting informed choice regarding health and reproductive decisions
- Advocating for privacy, confidentiality, and nondiscrimination of genetic information

The International Society of Nurses in Genetics (ISONG), which was incorporated in 1987, is the professional society for registered nurses specializing in genetics.[150] ISONG's goals are to promote the integration of nursing process into the delivery of genetic health care, to encourage the incorporation of the principles of human genetics into all levels of nursing education, to promote the development of standards of practice for nurses in human genetics, and to support advancement of nursing research in human genetics.[151]

In 1998, ISONG, in collaboration with the ANA, issued the "Statement on the Scope and Standards of Genetics Clinical Nursing Practice," which delineates the standards of care and standards of professional performance for genetics clinical nursing practice.[152] The ISONG-ANA statement distinguishes between basic and advanced genetics nursing practice.[153] Basic level genetics nurses are responsible for assessment, plan of care, intervention, and evaluation. They "require either formal genetics clinical experiences through their R.N. preparatory programs or on-the-job training in their specified role under the supervision of a professional trained in genetics."[154] Advanced genetics nurses are licensed registered nurses who, at minimum, have (1) successfully completed an accredited graduate program in nursing, (2) completed graduate-level genetics course work,[155] and (3) participated in genetics clinical training supervised by any combination of the following: (a) graduate nursing faculty, (b) genetics advanced practice nurses, or (c) board-certified geneticists.[156] Advanced genetics nurses should have expanded skills that include pedigree construction; genetic physical assessment and dysmorphology examination; comprehensive, disease-specific health and family histories; interpretation of complex genetics laboratory data and test results; management of genetic therapeutic modalities; and genetic counseling.[157]

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[150] Ibid., 19.

[151] Ibid.; International Society of Nurses in Genetics, "About ISONG," website: *http://nursing.creighton.edu/special/isong2/About_isong/Index.html*, visited January 12, 2000.

[152] International Society of Nurses in Genetics, Inc., and American Nurses Association, *Scope and Standards of Genetics Clinical Nursing Practice*.

[153] Ibid., 4.

[154] Ibid., 5.

[155] Graduate-level genetics course work should include human, molecular, biochemical, and population genetics content; technological applications; therapeutic modalities; and ethical, legal, and social implications of genetics information and technology. Ibid., 6.

[156] Ibid.

[157] Ibid., 6–7.

### Oncology Nurses

Among the medical specialties, oncology is unique in that advances in understanding of cancer biology and the expanding role of genetics in the development of cancer are rapidly changing cancer medicine and nursing practice.[158] Gene variants that increase risk for several familial cancer syndromes, such as breast and ovarian hereditary cancer syndrome and hereditary nonpolyposis colorectal cancer, have been identified, and predictive genetic testing is available. However, questions about a test's clinical predictive value for different individuals still exist, and there may be limits to a test's clinical utility.[159] The uncertainties are caused, in part, by the fact that the consequences of some mutations within a gene are currently unknown and the degree to which genetic and nongenetic factors contribute to the development of cancer varies with the type of cancer and with the particular individual's personal and family medical histories. Thus, it is especially important that patients receive pretest counseling and posttest results and counseling from knowledgeable clinicians.[160] For this reason, oncology nurses must have a basic understanding of genetics, incorporate genetic risk assessment into their practices, and be knowledgeable about advances in cancer predisposition genetic testing.[161]

Many commentators believe that as additional cancer predisposition gene variants continue to be identified, oncology nurses will play a vital role in assessing clients for increased risk of developing cancer, educating clients about the availability of predisposition genetic testing, counseling clients, and making referrals for cancer genetic counseling and risk assessment.[162] The Oncology Nursing Society has formed a genetics project team to develop and implement genetic education strategies.[163]

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[158] For example, in a statement on genetic testing for cancer susceptibility, the Society for Surgical Oncology endorses reform in four important areas involving genetic testing: clinical patient care, medical education, research, and patient rights or advocacy. V. S. Klimberg et al., "Society of Surgical Oncology: Statement on Genetic Testing for Cancer Susceptibility," *Annals of Surgical Oncology* 6, no. 5 (1999): 507–509.

[159] See Chapter 3, page 63, and Chapter 5, page 126; see also P. T. Rieger, "Overview of Cancer and Genetics: Implications for Nurse Practitioners," *Nurse Practitioner Forum* 9, no. 3 (1998): 122, 126.

[160] Ibid.

[161] Ibid., 122, 126, 128–1230.

[162] See ibid.; L. J. Loescher, "The Family History Component of Cancer Genetic Risk Counseling," *Cancer Nursing* 22, no. 1 (1999): 96–102; D. J. MacDonald, "The Oncology Nurse's Role in Cancer Risk Assessment and Counseling," *Seminars in Oncology Nursing* 13 (1997): 123–128; L. J. Loescher, "Genetics in Cancer Prediction, Screening, and Counseling: Part II, The Nurse's Role in Genetic Counseling," *Oncology Nursing Forum* 22, no. 2 Supp. (1995): 16–9.

[163] J. Jenkins, "Educational Issues Related to Cancer Genetics," *Seminars in Oncology Nursing* 13 (1997): 141, 143.

### Other Nursing Professionals

Other nursing professionals' training and practices also are affected by advances in medical genetics. Both genetics and nursing professional organizations recognize the expanding role of nurses in genetics services and the growing need for nursing professionals to be trained in genetic counseling. However, according to a group of nursing experts who called for integration of genetic science into all levels of nursing education and research, nurses are not being academically or clinically prepared at a rate that parallels this need.[164] A survey of nursing specialty organizations associated with the Nursing Organization Liaison Forum found that 70 percent of the respondents were not planning any educational offerings in genetics, and no respondents indicated an interest in providing their members with consumer perspectives on genetics and genetic risk or illness in their families.[165]

The ANA view is that nurses will need simultaneously to update their genetic knowledge, comprehend the multifaceted impact of genetic information, and anticipate future trends.[166] In 1993, the ANA began work on the project "Managing Genetic Information: Policies for U.S. Nurses," funded by the ELSI Branch of the National Center for Human Genome Research, to assess ways in which nurses in the United States are currently managing genetic information.[167] Under the project, the ANA conducted a national survey of 1,000 practicing nurses that examined their attitudes, concerns, and experiences with genetic testing, counseling, and referral.[168] The results of this survey showed that nurses have limited education in genetics but are already providing care to individuals who have genetic disorders on a regular basis, despite the nurses' lack of confidence in their own level of genetic knowledge.[169] Only 9 percent of the respondents had taken a genetics course during their basic education, while a majority had seen clients who had requested genetic information or who had been referred for genetic counseling, screening, or testing.[170] The nurses in the survey realized that current genetic efforts are significant to their practice and recognized the need for increased education and research in genetics.[171] The ANA's report on the project emphasized the importance of developing guidelines for using genetic information, understanding the impact of this information on nurse-client relationships, and developing standards for client education.[172]

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[164] Monsen and Anderson, "Continuing Education for Nurses," 21. See also Hayflick and Eiff, "Role of Primary Care Providers," 20 ("In nursing, there is widespread recognition of the lack of adequate genetics education for most nurses.").

[165] Monsen and Anderson, "Continuing Education for Nurses," 23.

[166] C. Scanlon and W. Fibison, *Managing Genetic Information: Implications for Nursing Practice* (Washington, D.C.: American Nurses Association, 1995), 36.

[167] Ibid., 2–3.

[168] Ibid., 2–4, 45–57.

[169] Ibid.; National Human Genome Research Institute, "Review of the Ethical, Legal and Social Implications Research Program and Related Activities (1900–1995)," website: *http://www.nhgri.nih.gov/About_NHGRI/Der/Elsi/elsi_review.html*, visited December 16, 1999.

[170] Scanlon and Fibison, *Managing Genetic Information*, 45–57.

[171] Scanlon and Fibison, *Managing Genetic Information*, 5.

[172] Ibid., 3.

Based on the survey results, the ANA developed recommendations for nursing practice, education, research, and policy in furtherance of its goal to ensure the quality of genetics services and genetic competence of nurses. The nineteen specific recommendations[173] include:

- Developing professional guidelines and standards
- Providing practice-based education to develop nurses' skill and expertise in managing genetic information
- Providing education on genetic issues
- Requiring a fundamental genetics course during preclinical nursing preparation
- Expanding the availability of graduate education programs for nurses who wish to specialize in genetics
- Establishing continuing education in genetics
- Supporting nursing research in genetics and the role of nurses in the delivery of genetics services and the management of genetic information
- Encouraging nurses to participate in professional and public dialogue on genetics issues

The ANA also developed guidelines for nursing practice on issues of informed consent, privacy and confidentiality, truth-telling and disclosure, and nondiscrimination.[174] At a 1999 meeting, the ANA House of Delegates addressed "the need for nurses to have a strong knowledge base in genetics to be able to accurately assess, provide information, and make referrals for patients and families with genetic concerns."[175] The ANA House of Delegates adopted the recommendations that the ANA: (1) "promote the inclusion of information about genetics in basic, advanced, and continuing nursing education programming"; (2) "promote dissemination of information about genetic discoveries and their applications in health care"; and (3) "advocate to

[173] Ibid., 38–39.
[174] Ibid., 15–35.
[175] American Nurses Association, 1999 ANA House of Delegates, Washington, D.C. (June 17–20, 1999), website: *http://www.nursingworld.org/about/summary/sum99/genetics.htm*, visited December 16, 1999.

reduce discrimination toward persons and families with and/or at risk for a condition with a genetic component."[176]

The NHGRI's Medical Genetics Branch has a Genetic Nursing Section, whose mission is to model the incorporation of genetics into the professional role of nursing and to facilitate the process of preparing nurses to provide genetics services.[177] The Genetic Nursing Section has set forth seven goals to achieve its mission and has developed initiatives and events sponsored by the nurses at NHGRI in collaboration with others, such as fellowships, workshops, and continuing education programs, to implement those goals.[178]

**Other Health Professionals**

In addition to professionals in medicine and nursing, other "allied health" professionals perform essential work in a variety of health care professions, such as physical therapy, medical technology, occupational therapy, health information management, health care administration, physician assistant studies, and respiratory care. They provide indispensable assistance and support to physicians and nurses in delivering health care services to patients. Thus, in the emerging era of genomic medicine, allied health professionals in all areas of health care will have an increasing role in providing genetics services to patients and should have a basic understanding of genetics.

Under a three-year grant from the NHGRI, the members of the Human Genome Education Model Project (HuGEM) team began in 1997 the HuGEM II Project to address the genetics education needs of allied health professionals through their national organizations.[179] Building on the experiences and products of the HuGEM I project (1993–

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[176] Ibid.

[177] National Human Genome Research Institute, "Genetic Nursing Section," website: *http://www.nhgri.nih.gov/Intramural_research/Medical_genetics/Genetic_nursing/index.html*, visited December 16, 1999.

[178] Ibid. The Genetic Nursing Section's seven mission goals are:

1. Preparing health care professionals to incorporate human genetics into their professional roles and responsibilities
2. Collaborating with professional nursing societies to plan for development of guidelines, standards, and education of their members
3. Facilitating the incorporation of human genetics into nursing school curriculum to promote basic genetic knowledge of all graduating nurses
4. Utilizing computer resources to provide access to genetics information
5. Providing an optimum learning environment while delivering quality care in the genetics clinic
6. Implementing research projects that will impact educational, clinical, and administrative decisions related to genetics health care
7. Training programs

[179] Human Genome Education Model Project II website: *http://www.dml.georgetown.edu/hugem/introduc.html*, visited February 14, 2000; "HuGEM to Educate Health Professionals in Genetics," *Human Genome News* 9, no. 1–2 (1998), 12. The collaborating professional organizations are: American Dietetic

1997), the purpose of the HuGEM II Project is to provide educational training and resources to increase the knowledge of and sensitivity to human genetics, the Human Genome Project, and the ethical, legal, and psychosocial issues of genetic testing and research. The educational phase of HuGEM II includes educational workshops conducted at national, regional, and state conferences of the collaborating organizations.

## Payment for Genetics Services

### How Medical Services Are Billed

#### *CPT Codes*

Health providers and third-party payers (e.g., health care insurers) use a system of standardized codes for purposes of reimbursing medical services. The coding system consists of International Classification of Diseases (ICD-9) codes, which indicate the reason for the patient's visit,[180] and Current Procedural Terminology (CPT) codes, which indicate the medical procedure the health provider performed.[181] The existence of a CPT code, however, does not guarantee reimbursement. Each third-party payer sets additional guidelines to determine which CPT codes are covered.

CPT codes were first developed and published by the AMA in 1966 to systematize the terms used by health providers so that they could better communicate among themselves.[182] The CPT codes are updated annually by review of an AMA physician editorial panel.[183] In the 1980s, the Health Care Financing Administration adopted the CPT codes as part of its Common Procedure Coding System (HCPCS) and mandated the use of HCPCS for Medicare and Medicaid reimbursement.[184] Consequently, the majority of private third-party payers also began using the CPT codes for reimbursement,[185] and the CPT codes have become the "most universally accepted system" to identify medical services for reimbursement.[186]

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Association, American Occupational Therapy Association, American Physical Therapy Association, American Psychological Association, American Speech-Language-Hearing Association, Council on Social Work Education, and National Association of Social Workers.

[180] M. K. Beard, "The Impact of Changes in Health Care Provider Reimbursement Systems on Recovery of Damages for Medical Expenses in Personal Injury Suits," *American Journal of Trial Advocacy* 21 (1998): 453, 479–480. A reorganization of the ICD-9 codes, referred to as ICD-10 codes, has been proposed but has not yet been adopted. Telephone interview with Celeste Curshner, June 15, 1999; American Health Information Management Association, Chicago, IL, website: *http://www.ahima.org/publications/2g/coding.notes/598.html*, visited June 14, 1999.

[181] American Medical Association website: *http://www.ama-assn.org/med-sci/pt/ process.html*, visited April 26, 1999.

[182] American Medical Association website: *http://www.ama-assn.org/med-sci/pt/process.html*, visited April 26, 1999.

[183] Ibid. (explanation of amendment procedure).

[184] Ibid.; W. W. Grody and M. S. Watson, "Those Elusive Molecular Diagnostic CPT Codes," *Diagnostic Molecular Pathology* 6, no. 3 (1997): 131, 131.

[185] American Medical Association website: *http://www.ama-assn.org/med-sci/pt/process.html*, visited April 26, 1999.

[186] Grody and Watson, "Elusive Molecular Diagnostic CPT Codes," 131.

### *CPT Codes for Genetics Services*

The AMA has recently expanded the CPT codes for genetic testing.[187] The major developments occurred in 1998 when the AMA added twenty-eight CPT codes to the existing five codes applicable for genetic testing.[188] In 1999, the CPT codes were further expanded and edited.[189] Most practitioners agree that the 1999 codes for genetic testing are an improvement over previous codes and are sufficiently specific to accurately reflect the medical services provided.[190]

### *Proposed CPT Codes for Genetic Counseling*

In 1995, the genetics community proposed a five-tiered coding structure for genetic counseling that would reimburse based on the complexity and duration of the counseling.[191] Finding the current consultation codes adequate, the AMA has thus far decided against the adoption of CPT codes for genetic counseling.[192] More recently, the ACMG has submitted proposals to the AMA CPT Advisory Committee to develop CPT codes for "Patient Education and Counseling, under the direction of, but not necessarily by a physician."[193] The Advisory Committee may decide to submit the proposed codes to the full editorial panel for review.[194] Some states have adopted their own coding system to supplement the CPT codes in order to include coding for genetic testing.[195] Proponents of CPT codes for genetic counseling, mindful of the AMA's past reservations, are also formulating a single "risk assessment/pedigree development" code that would account for the "substantive component" of genetic counseling.[196]

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[187] For an overview of the development of genetic testing CPT codes, see Grody and Watson, "Elusive Molecular Diagnostic CPT Codes," 131–132.

[188] American College of Medical Genetics, "CPT Coding Revisions," *Genetics in Medicine* 1 (1999): 112, 114–116.

[189] Ibid., 112, 114–116.

[190] American College of Medical Genetics, *Genetics in Medicine* 1, no. 3 (March/April 1999); Grody and Watson, "Elusive Molecular Diagnostic CPT Codes," 131–132 (speaking of the 1998 codes).

[191] D. L. Doyle, "CPT Code for Our Services? Not Yet…," *Perspectives in Genetic Counseling* 18, no. 2 (1996): 5, 5; B. Bernhardt, B. N. Peshkin, and Y. Kemel, "Billing and Record-Keeping for Familial Cancer Risk Counseling: A National Survey," *Journal of Genetic Counseling* 7, no. 4 (1998): 317, 318; M. Watson, "National Coding for Genetic Services," presentation at the Council of Regional Networks for Genetic Services meeting, Washington, D.C., February 16–17, 1996.

[192] Bernhardt, Peshkin, and Kemel, "Billing and Record-Keeping for Familial Cancer Risk Counseling," 318.

[193] D. B. Flannery, "Report of the Committee on Economics of Genetic Services," American College of Medical Genetics website: *http://www.faseb.org/genetics/acmg/contrep2.htm*, visited May 11, 1999.

[194] Telephone interview with Deborah Lochner Doyle, State Coordinator for Genetic Services, Seattle, WA, November 1998.

[195] For example, Ohio adopted a series of genetic counseling codes that classify certain types of counseling sessions, such as "pedigree construction, initial"; "medical genetic counseling, follow-up"; and "psychological genetic counseling, complex." Ohio currently has eight separate codes for counseling and is contemplating expanding the program to include reimbursement for testing, which is currently conducted at genetic services centers throughout the state. Telephone interview with Shelley L. Nottingham, Bureau of Early Intervention Services, Ohio Department of Health, Columbus, Ohio, June 22, 1999; excerpts from Medicaid reimbursement manual.

[196] Telephone interview with Dr. Michael S. Watson, Ph.D., Professor, Washington University in St. Louis, MO, June 14, 1999.

Although there are no CPT codes for genetic counseling, physicians and medical geneticists can seek reimbursement for counseling services by using general consultation codes.[197] However, because there are no CPT codes specifically for genetic counseling, many third-party payers may not reimburse for the counseling, may do so inconsistently, or may reimburse at a lower rate or less often for counseling than for medical services.[198] In addition, insurers may restrict the amount of reimbursement by, for example, limiting the amount of time for each consultation.[199]

Without CPT codes that relate specifically to genetic counseling by nonphysician counselors, genetic counselors who are not physicians cannot bill the insurers directly for the counseling they provide. Moreover, since genetic counselors are not licensed or certified by states, third-party payers do not regard them as reimbursable providers.[200] Instead, their services must be billed through or under the name of a supervising physician.[201] Some genetic counselors have expressed reservations about billing through a physician when the physician's involvement in the counseling has been minimal.[202] Moreover, since many insurers refuse to pay for genetic counseling even when such services are billed under the name of a physician, many institutions do not even bill for genetic counselors' services in order to avoid expending administrative resources to obtain reimbursement that probably would be insufficient to cover such costs.[203] Consequently, most genetic counseling activities are not self-supporting because they are undercompensated for labor-intensive and time-consuming services.[204]

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[197] Bernhardt, Peshkin, and Kemel, "Billing and Record-Keeping for Familial Cancer Risk Counseling," 322 (57 percent of study population used consultation codes for billing when seeing a new patient.); Telephone interviews with Luba Djirjinovic and Karen Brown, May 5, 1999.

[198] Bernhardt and Pyeritz, "The Economics of Clinical Genetics Services. III," 291.

[199] Some practitioners simply ask their patients to return for multiple visits and bill for a separate consultation each time. Other practitioners who prefer longer office visits regret forcing clients to return multiple times. For conditions that require extended family participation, traveling to the medical geneticists or counselors multiple times may present a hardship. Telephone interview with Dr. Michael S. Watson, Ph.D., Professor, Washington University in St. Louis, MO, June 14, 1999.

[200] Bernhardt and Pyeritz, "The Economics of Clinical Genetics Services. III," 291.

[201] Ibid., 292–293. One genetic counselor reported that some institutions bill genetic counseling services as "technical fees," such as "room charges." Meeting of genetic counselors with Task Force staff on May 5, 1999.

[202] Telephone interview with Karen Brown, May 5, 1999; Bernhardt, Peshkin, and Kemel, "Billing and Record-Keeping for Familial Cancer Risk Counseling," 327.

[203] Meeting of genetic counselors with Task Force staff on May 5, 1999; B. Bernhardt, B. N. Peshkin, and Y. Kemel, "Billing for Familial Cancer Risk Counseling (FCRC): A National Survey," Abstract for the October 1997 Annual Meeting of the American Society of Human Genetics.

[204] See B. A. Bernhardt, J. E. Tumpson, and R. E. Pyeritz, "The Economics of Clinical Genetics Services: IV. Financial Impact of Outpatient Genetic Services on an Academic Institution," *American Journal of Human Genetics* 50 (1992): 84–91; Bernhardt and Pyeritz, "The Economics of Clinical Genetics Services: III," 288–293; Bernhardt et al., "The Economics of Clinical Genetics Services: II," 559–565; R. E. Pyeritz, J. E. Tumpson, and B. A. Bernhardt, "The Economics of Clinical Genetics Services: I. Preview," *American Journal of Human Genetics* 41 (1987): 549–558. According to one genetic counselor, board-certified

## Insurance Coverage of Predictive Genetic Testing

### *National Coverage of Testing*

Insurance coverage is a key factor affecting the dissemination and use of clinical laboratory services. There is evidence that in the last five years, since the first appearance of BRCA gene testing, insurers are moving toward coverage of genetic susceptibility testing for patients at identified genetic risk for common complex disorders of adulthood. For example, whereas a 1996 national survey found that approximately one quarter of health maintenance organizations (HMOs) were covering BRCA gene testing on a case-by-case basis,[205] the major commercial laboratory for BRCA testing now reports that almost all major insurers, including HMOs, pay for BRCA testing of high-risk women.[206]

There also is evidence for increased coverage of other predictive genetic tests. Some commentators predict that increasing clinical validity and utility data for genetic tests and development of professional guidelines will promote further coverage.[207] Insurers surveyed in 1996 thought that coverage of both BRCA testing and cystic fibrosis reproductive carrier screening "would be increased significantly if the group tested was restricted to those at high risk, if detection rates were higher and costs lower, and if testing was endorsed by a national professional group or consensus conference." [208]

In a 1996 survey, most HMO medical directors responded that they would consider development of policies for predictive genetic testing within five years.[209] Some large HMOs and other insurers have since established policies for the medical appropriateness of BRCA

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genetic counselors generally are not compensated at a higher rate than genetic counselors who are not board-certified. Randi Zinberg, M.S., Genetic Counselor, Department of Human Genetics, Mount Sinai School of Medicine of the New York University, New York, NY, presentation to the New York State Task Force on Life and the Law, May 26, 1999.

[205] M. F. Myers, T. Doksum, and N. A. Holtzman, "Genetic Services for Common Complex Disorders: Surveys of Health Maintenance Organizations and Academic Genetic Centers," *Genetics in Medicine* 1 (1999): 272.

[206] Myriad Genetics, Inc., website: *http://www.myriad.com/gtpatbq.r.html*, visited June 1, 2000; see also P. A. Manley, R. J. Pennel, and T. S. Frank, "Insurance Reimbursement for BRCA1 and BRCA2 Sequence Analysis" (abstract), *Journal of Genetic Counseling* 7 (1998): 462. In reaction to the initial low consumer demand for BRCA testing, which Myriad later determined was influenced by worries about insurance coverage, genetic discrimination and the limited usefulness of test results, Myriad began a marketing campaign that included forging agreements with major insurance companies to cover BRCA testing, providing counseling literature, funding the AMA to write a primer for physicians on the benefits of BRCA testing, and promoting research to study the usefulness of BRCA testing. S. Lehrman, "Selling the Breast Cancer Susceptibility Test," *GeneLetter* (April 2000), website: *http://www.geneletter.com*, visited July 18, 2000.

[207] Telephone interview with Dr. Alan Bombard, Director Medical Director, West Region, Women's Health, Aetna U.S. Healthcare, San Ramon, CA, June 11, 1999; for a discussion, see M. M. Schoonmaker, B. A. Bernhardt, and N. A. Holtzman, "Factors Influencing Health Insurers' Decisions to Cover New Genetic Technologies," *International Journal of Technology Assessment in Health Care* 16 (2000): 178.

[208] Schoonmaker, Bernhardt, and Holtzman, "Factors Influencing Health Insurers' Decisions to Cover New Genetic Technologies," 178, 186.

[209] Myers, Doksum, and Holtzman, "Genetic Services for Common Complex Disorders," 275, 278.

testing and other predictive genetic testing.[210] Insurers have been guided in turn by professional guidelines, including 1996 American Society of Clinical Oncology guidelines for cancer susceptibility testing[211] and guidelines for reproductive screening tests produced by the American College of Obstetricians and Gynecologists (ACOG).[212]

## Coverage of Testing by New York State Insurers

In the summer of 1999, Task Force staff conducted a survey of representative insurers operating in New York State to determine coverage policies and practices for predictive genetic testing. The Task Force surveyed twelve insurers, eight of whom responded. Respondents provided insurance by indemnity plans, preferred provider organizations, HMOs, and Medicaid managed care.[213] The survey assessed coverage practices for predictive testing of healthy adults for late-onset disorders (presymptomatic testing for Huntington disease and familial colon cancer and BRCA testing) and reproductive carrier screening (for Tay-Sachs disease and Gaucher disease).[214]

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[210] Blue Cross and Blue Shield Association Technology Evaluation Center, Tech Assessment on Genetic Testing for Inherited BRCA1 or BRCA2 Mutations (Blue Cross Blue Shield, Washington, D.C., 1997); J. Reiss et al., "Implementation of an Inherited Breast/Ovarian Cancer Susceptibility Clinical Practice Guideline: Who Receives Counseling, and Who Is Interested in Genetic Testing?" Presentation at American Society of Human Genetics Annual Meeting, San Francisco, October, 19–23, 1999; telephone interview with Dr. Alan Bombard, Director Medical Director, West Region, Women's Health, Aetna U.S. Healthcare, San Ramon, CA, June 11, 1999.

[211] American Society of Clinical Oncology, "Statement of the American Society of Clinical Oncology: Genetic Testing for Cancer Susceptibility," *Journal of Clinical Oncology* 14 (1996): 1730.

[212] ACOG issues guidelines for reproductive genetic tests that are widely regarded as standards of care. The college has, for example, issued guidelines for reproductive carrier screening for Tay-Sachs disease but not for Gaucher disease. For a discussion, see Chapter 5, pages 129–130.

[213] Insurers were selected after consulting with the New York State Department of Health. The Task Force contacted each insurer and spoke with the Medical Director, or equivalent. Insurers that agreed to participate were then mailed a copy of the survey in anticipation of a telephone interview during which a member of the Task Force staff read each question and recorded the insurer's answer. Additionally, some insurers provided the Task Force with copies of specific policies. The survey asked if specific tests would be covered under specific circumstances. All questions about testing policies were prefaced with the phrase, "Assuming coverage is not excluded by the employer contract . . . "

[214] These conditions were selected because they raise different issues. Presymptomatic testing for both Huntington disease and familial adenomatous polyposis (FAP) colon cancer predict future disease with almost 100 percent certitude; FAP, but not Huntington disease, can be prevented by medical surveillance and intervention. BRCA susceptibility testing provides probabilistic risk information; preventive interventions exist but are more complicated (see Chapter 3, page 63). Reproductive carrier screening for both Tay-Sachs disease and Gaucher disease target those at high risk for affected offspring but symptom

Survey results show that insurers generally reimburse for both adult-onset testing and carrier screening tests as medically appropriate. In the absence of coverage policies, most insurers made decisions on a case-by-case basis. However, many insurers indicated that they have developed or are developing coverage guidelines. Several insurers cited policy statements by professional organizations as the primary reason why they had developed reimbursement policies for specific genetic disorders.[215] Another factor prompting policy development is the volume of test requests;[216] for example, although all insurers answered that they would cover Huntington disease testing based on family history, some insurers were not aware that requests for testing had been received.

All surveyed insurers cover BRCA testing, but they differ in the conditions of coverage and in who was considered medically appropriate for testing. Some insurers require a minimal number of affected relatives, while others leave the determination of medical appropriateness to the individual physician. Some, but not all, will cover testing of an insured person who has already received a diagnosis of breast or ovarian cancer. At least one insurer will cover testing of an affected family member of the at-risk insured for the enefit of the latter, even though the affected member does not have a policy with that insurer.[217]

Insurers also generally cover preconception and prenatal carrier screening for both Tay-Sachs disease and Gaucher disease for persons at reproductive risk based on ethnic background. Several insurers stated that ACOG and ACMG guidelines are important in establishing their company coverage policies. For example, one insurer was unaware of requests for Gaucher disease screening but questioned the appropriateness of screening since, unlike Tay-Sachs disease screening, it is not a recognized standard of care. Some, but not all, insurers will cover testing of an uninsured reproductive partner of the insured, even though testing the partner of an insured who tests positive is critical to the reproductive testing process and outcome.[218]

All surveyed insurers cover genetic counseling for predictive genetic testing. Even when the insurer does not reimburse for the laboratory test itself, the policy covers genetic counseling so those individuals can assess whether to undergo testing. In general,

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severity and expression vary considerably for the two tests. ACOG recommends reproductive carrier screening for Tay-Sachs disease for certain population groups but it has not issued guidelines for carrier screening for Gaucher disease. See also Chapter 5, pages 129–130.

[215] Other, less frequent, responses included New York State Department of Health test designation as investigational rather than generally accepted (see Chapter 11, page 323), employer willingness to pay for the service, insured requests for coverage, and the policies of other insurers.

[216] See also Schoonmaker, Bernhardt, and Holtzman, "Factors Influencing Health Insurers' Decisions to Cover New Genetic Technologies," 187.

[217] For BRCA testing, it is preferable to first test a family member who has had breast or ovarian cancer to identify a family mutation. For a discussion, see Chapter 3, page 63.

[218] Some clinical geneticists informed Task Force staff of actual cases in which insurers would not cover reproductive testing of male partners when testing was clearly warranted and might not otherwise occur. In some cases refusal to cover testing may have been due to failure to understand risk through paternal genetic transmission.

insurance policies express a preference for counseling by medical geneticists with a M.D. or D.O. degree.[219] Some insurers permit counseling by Ph.D. geneticists or nongeneticist physicians but are reluctant to cover counseling by nonphysician or non-Ph.D. genetic counselors. Insurers that cover counseling by genetic counselors require a supervising physician to bill for the counseling services.[220]

## Conclusions and Recommendations

### State Licensure or Certification of Genetic Counselors

**To ensure an adequate level of competency of genetic counselors and to support the viability of the profession of genetic counseling, New York State should create a process for state certification of genetic counselors who are certified by the American Board of Genetic Counseling or American Board of Medical Genetics.**

Unlike other health professionals and practices, genetic counseling is not a profession regulated by state law. Although the ABGC has established requirements for graduate programs and board certification of genetic counselors, such requirements are voluntary and not mandated under state law; thus, any individual can claim to be and practice as a genetic counselor. Since demand for genetic counseling services will likely increase with advances in medical genetics, there is concern that the number of genetic counselors without adequate training and board certification will rise.

In addition, many genetic counselors have difficulty obtaining reimbursement from third-party payers. Absent a revision of the CPT codes to include genetic counseling services by nonphysician counselors, third-party payers may be more likely to fully reimburse genetic counseling services if genetic counselors are licensed or certified professionals under state law.

At this time, there appear to be too few genetic counselors in the state to justify the high costs of a state licensing board for genetic counseling. In addition, in light of prior unsuccessful efforts to license genetic counselors, there may be additional barriers, other than cost considerations, that make licensing genetic counselors unfeasible. However, state certification of genetic counselors would achieve many of the principal goals of licensure without the expense of a separate state licensing board. Given the importance of ensuring access to reliable and competent genetic counseling in New York

[219] Insurers did not indicate a preference that the physician be certified by the American Board of Medical Geneticists.

[220] One insurer, however, described such a practice as "fraudulent" and expected that any counseling billed by a physician should be conducted by that physician.

State, we recommend that New York enact legislation authorizing state certification of genetic counselors who are certified by the ABGC or the ABMG.

**Scope of Genetic Counseling Practice**

**Ideally, all genetic counselors should work within a team of health care providers, which may include medical geneticists, Ph.D. geneticists, primary care physicians, and physician specialists, such as oncologists, obstetrician-gynecologists, and neonatologists, to provide genetic counseling as an integrated component of the patient's health care. If genetic counselors practice independently, they should maintain the same level of professional standards as genetic counselors who work within institutional settings and should strive to achieve the benefits of working in an integrated health care team by consulting with other genetics and nongenetics professionals.**

Since genetic counseling is an essential element of all genetics services, genetic counselors' services are most beneficial to patients when they are provided within the context of overall health care. Thus, ideally, all genetic counselors should work within a team of health care providers, which may include medical geneticists, Ph.D. geneticists, primary care physicians, and physician specialists, such as oncologists, obstetrician-gynecologists, and neonatologists, to provide genetic counseling as an integrated component of the patient's health care. They should interact and consult with other genetics and nongenetics health professionals to coordinate health care for their patients.

We recognize, however, that there are circumstances in which genetic counselors may want or find it necessary to practice independently. For example, genetic counselors who are located in rural areas without a major medical center may not be able to work within a health care team of a single medical institution. Genetic counselors in such locations might set up an independent practice to provide genetic counseling services to patients. Nevertheless, genetic counselors who practice independently should still maintain the same level of professional standards as genetic counselors who work within institutional settings. In such circumstances, even though other health care professionals are located in different and perhaps distant settings, genetic counselors who practice independently should strive to achieve the benefits of working within an integrated health care team by consulting and, if necessary, coordinating counseling services with the patient's other health care providers and consulting with appropriate genetics professionals.

Genetic counselors should not practice independently unless they have had sufficient clinical training and experience. Professional societies for genetic counselors, such as the ABGC and the NSGC, should consider establishing standards, including internship and/or residency requirements, for genetic counselors who seek to practice independently.

### Authorization to Order Genetic Tests

**Under New York law, genetic counselors can order genetic testing for their patients only through licensed physicians or other persons who are authorized by law to do so, such as dentists, podiatrists, and nurse practitioners. The Task Force does not recommend any changes to the current law.**

Currently, genetic counselors in New York are not permitted to order genetic testing. Although some genetic counselors support a change in this policy, many commentators contend that the ability to order genetic testing would allow genetic counselors to practice medicine without a medical license because the determination of whether to order genetic testing would require at least some medical diagnostic evaluation on the part of the genetic counselor. Also, because of the complexity of genetic test information and the continuous evolution of test-specific clinical validity and utility data, physicians who are not genetics specialists and who order genetic tests should refer patients, when appropriate, to clinical genetics specialists, including genetic counselors, for pretest and/or posttest counseling. In light of these concerns, the Task Force believes that only physicians or other appropriately licensed professionals should be allowed to order genetic tests and does not recommend legislation or regulations to permit nonphysician genetic counselors to order genetic testing.

### Direct Billing by Genetic Counselors

**The Task Force encourages the American Medical Association to adopt changes to the CPT codes that would allow nonphysician genetic counselors to bill directly for genetic counseling services.**

Based on our research and discussions with practitioners, genetic counselors, and third-party payers, we conclude that most genetic counselors are underreimbursed by third-party payers. At present, there are no CPT codes for genetic counseling by nonphysician counselors; third-party payers reimburse some counseling services only if a supervising physician bills them as consultations. This undercompensation creates a financial disincentive to enter the genetic counseling profession and may cause or aggravate a shortage, as some commentators have predicted, of board-certified genetic counselors in the future. Therefore, we strongly encourage the AMA to revise the CPT codes to allow nonphysician genetic counselors to bill directly for genetic counseling services.

### Training Genetic Counselors about Legal and Ethical Issues

**All genetic counselors should receive training in and be knowledgeable about legal and ethical issues relevant to genetic counseling, such as confidentiality and medical privacy. Professional societies of genetic**

**counselors should develop standards and guidelines for educating and training genetic counselors about legal and ethical issues.**

Neither the NSGC's code of ethics nor the ABGC's accreditation requirements for graduate programs discuss or require training in legal and ethical issues relevant to genetic counseling, such as confidentiality, medical privacy, and the use of genetic information by employers and insurers. Based on our research and discussions with practitioners, it appears that many genetic counselors do not consider themselves to be sufficiently knowledgeable to address legal and ethical issues and are uncomfortable dealing with questions on such issues from their clients. While board-certified genetic counselors may gain some knowledge about legal and ethical issues through their clinical experience, such training is ad hoc and necessarily incomplete, and there is concern among practitioners that genetic counselors are not properly trained about legal and ethical issues to counsel their clients.[221] Thus, professional societies should develop guidelines and standards for educating and training genetic counselors on legal and ethical issues relevant to genetic counseling.

### Genetics Training in Medical School and Postgraduate Education

**Medical schools should incorporate genetics education into their core curriculum. Medical schools and postgraduate training programs should integrate genetics into clinical practice training to teach the necessary skills and attitudes for recognition and assessment of the genetic component of disease.**

In the era of genomic medicine, genetics will have a tremendous impact on all areas of medicine, and physicians in all areas will need to have a basic knowledge of genetics. Ideally, all physicians should receive genetics education and training in medical school and postgraduate programs. Yet despite the rapid growth in genetics technology, most medical schools and postgraduate programs have not yet incorporated genetics curricula into medical education and training. We urge medical schools to incorporate genetics education into their core curricula. Medical schools and postgraduate training programs should integrate genetics into clinical practice training to teach the necessary skills and attitudes for recognition and assessment of the genetic component of disease.

### Physician Licensure Examinations with Genetics Requirements

**Physician licensing examinations should assess knowledge of basic genetics issues.**

The likelihood that genetics will be covered in medical school and postgraduate training will improve if licensure examinations test medical students on genetics. We urge the National Board of Medical Examiners to ensure that these examinations include a sufficiently broad range of genetics questions to provide an incentive for medical schools and postgraduate programs to incorporate genetics into their curricula.

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[221] Meeting of genetic counselors with Task Force staff on May 5, 1999; see Tilley and Ormond, "Abstracts from the Seventeenth Annual Education Conference," 505 (abstract: N. Callanan et al., "The Challenge of Evolving Genetic Discrimination Policies: Lessons from a Six State Genetic Testing Project"); see also Chapter 10 for discussion of the use of genetic information in insurance and employment.

**Genetics Education through Clinical Guidelines**

**Professional medical associations should promote development of comprehensive and up-to-date clinical guidelines to help physicians recognize appropriate genetic testing opportunities, provide a source of continuing genetics education, and ensure that patients receive adequate counseling and appropriate specialty referrals. National and state health agencies and private partners should support the development, updating, and dissemination of professional guidelines.**

Clinical guidelines by genetics and other professional medical societies help practitioners keep abreast of new developments in genetics since they can be updated to reflect current medical understanding and technologies. Some genetics and other medical societies have already developed guidelines on genetic testing in certain specialty areas, such as oncology. In the era of genomic medicine, genetics should be integrated into clinical guidelines in all areas of medicine. Thus, professional medical associations should promote development of comprehensive and up-to-date clinical guidelines to help physicians recognize appropriate genetic testing opportunities, provide a source of continuing genetics education, and ensure that patients receive adequate counseling and appropriate specialty referrals. We encourage national and state health agencies and private partners to provide funding or other support to professional medical societies for the development, updating, and dissemination of professional guidelines.

**Specialty Board Certifications with Genetics Requirements**

**The American Board of Medical Specialties and the individual specialty boards should ensure that specialty board certification and recertification examinations adequately assess genetics competencies.**

Recent research reveals that specialty board examinations do not adequately assess genetics competencies. We agree with those commentators who have suggested that board examinations should provide more emphasis on genetics. We urge the ABMS and the individual specialty boards to ensure that specialty board certification and recertification examinations adequately assess genetics competencies.

**Medical Organization-Based Requirements for Genetics Education**

**Managed care and other medical practice organizations should promote genetics education of their member practitioners for the appropriate integration of genetic testing and counseling services and for specialty referrals.**

With the growth of managed health care, managed care and other medical practice organizations can be an effective means of educating their member providers on genetics. Managed care organizations should use their ability to influence medical practice to promote genetics education of their member practitioners for the appropriate integration of genetic testing and counseling services and for specialty referrals. The National Committee for Quality Assurance, a nonprofit organization that assesses and reports on the quality of managed care plans and accredits managed care organizations, should include genetics education and training as criteria in assessing and accrediting managed care organizations and provide information to consumers about the managed care organizations' policies on genetics education.

### Genetics Education and Training for Nursing and Allied Health Professionals

**Nursing and allied health professionals, working with the genetics community, should continue their efforts to incorporate genetics into all levels of nursing practice and allied health services and to promote research to assess and monitor the integration of genetics into all nursing and allied health practices.**

There is widespread recognition that most nursing and allied health training programs provide inadequate genetics education. At the same time, there has been a growing need to provide genetics services as a component of overall nursing care and allied health services. However, while some nursing and allied health programs have begun to incorporate genetics and genetics counseling, few nurses or allied health professionals are currently trained in genetics. Therefore, we encourage nursing and allied health professionals, working with the genetics community, to continue their efforts to incorporate genetics into all levels of nursing practice and allied health services and to promote research to assess and monitor the integration of genetics into all nursing and allied health practices.

## Summary of Legislative and Regulatory Recommendations

This report contains a variety of recommendations for changes in law, policy, and practice. This section summarizes the Task Force's recommendations for changes in statutes and regulations, all of which would require action by the legislature or executive

branch. The Task Force hopes that these recommendations will stimulate discussion and deliberation by lawmakers, practitioners, consumers, and other interested parties.

## Legislative Recommendations

### Genetic Screening

#### *Mandatory Genetic Screening*

- New York State should repeal legislation that mandates sickle cell screening for some couples seeking a marriage license.

### Newborn Screening

#### *Statutory Authorization for New York's Newborn Screening Program*

- New York Public Health Law § 2500-a should be amended to delete the names of individual disorders screened for by the Newborn Screening Program. The law should designate the Commissioner of Health to specify in regulations those congenital disorders for which screening should be performed.

#### *Mandatory Newborn Screening*

- New York's Newborn Screening Program should be mandatory for all infants born within the state, provided that several conditions are met: (1) all screening tests must meet the criteria described above in the recommendation concerning the basic requirements for newborn screening tests; (2) parents must be informed and receive educational materials about the program, its goals, and the screening process; and (3) the state must ensure that newborns identified as positive in screening tests are promptly diagnosed and that identified newborns and their families have access to follow-up medical care and counseling related to the disorder, regardless of their ability to pay. New York Public Health Law § 2500-a should be amended to remove the right of parents to assert religious objections to screening.

### Informed Consent

#### *Power of the Commissioner of Health*

- Those sections of New York's genetic testing statutes that list specific elements of informed consent should be replaced with an authorization for the

Commissioner of Health to issue regulations on the process and content of informed consent to predictive genetic testing.

*Court Orders for Predictive Genetic Testing*

- New York law should be amended to permit courts to order predictive genetic testing without the subject's consent only when (1) absent the testing, there would be a clear and imminent danger to the public health; (2) such testing is authorized by federal and/or New York State statutes or regulations; or (3) in a civil or criminal litigation, the subject affirmatively places his or her physical or mental condition at issue and the genetic testing directly relates to that physical or mental condition.

***Remedies for the Performance of Genetic Testing without Informed Consent***

- New York law should be amended to expressly authorize private lawsuits by subjects of unconsented-to predictive genetic tests against persons who order and/or perform the tests.

- New York law should be amended to authorize the Attorney General to bring lawsuits on behalf of individuals who have undergone predictive genetic testing without informed consent.

- Persons and organizations licensed by New York State should be subject to professional discipline and/or other sanctions, including fines and license suspension and revocation, for performing or ordering predictive genetic testing without informed consent.

***Research on Tissue Samples Obtained in the Clinical Setting***

- New York's law on the protection of human research subjects should be amended to cover research on tissue samples obtained in the clinical context. The amendment should apply only to tissue obtained after the amendment's effective date.

- Research on identified tissue samples obtained in the clinical context should be permitted only after the subjects have provided full informed consent to the research and an institutional review board has reviewed and approved the research protocol.
- Research on anonymized tissue samples obtained in the clinical context should be permitted only after an institutional review board has reviewed and approved the research protocol. The institutional review board review should ensure that the samples are or will be truly anonymized and should determine whether the research is of such a sensitive nature that it is inappropriate to use anonymized samples without having obtained the subjects' specific consent to the research.

- Research on coded tissue samples obtained in the clinical context should be permitted only if (1) the patients have agreed to the storage and research use of their coded samples; (2) the patients have been told about the operation, tissue release policies, and confidentiality protections of the tissue repository; and (3) an institutional review board has reviewed and approved the protocols for the research. The institutional review board review should ensure that the samples are or will be truly coded and should determine whether the research is of such a sensitive nature that it is inappropriate to use coded samples without having obtained the subjects' specific consent to the research. The coding of the samples should be performed by a person who is not connected to the research and who will not learn the individual results of the testing.

- Patients should be informed that their decision about whether to consent to the research use of their coded and/or identified tissue samples is wholly voluntary and that their decision will not affect their access to, or quality of, care.

## Predictive Genetic Testing of Children

### *Collection and Disclosure of Prospective Adoptees' Medical Histories*

- Parties placing a child for adoption should make reasonable efforts to collect a complete medical and genetic history of the child and provide it to the prospective adoptive parents. The parties also should make reasonable efforts to collect the medical and genetic histories of the birth parents and close blood relatives of the prospective adoptee and disclose them to the prospective adoptive parents. The parties should collect and disclose this information in a manner that respects the privacy of the persons from whom it is obtained and the subjects of the information.

## Confidentiality

### *Confidentiality Protections for Genetic Information and Other Medical Information*

- All personal medical information, including genetic information, should receive a uniform, high level of confidentiality protection. Absent new, comprehensive federal legislation or regulation that provides such protection, New York should enact comprehensive medical confidentiality legislation that does so.

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to protect the confidentiality of all genetic information.

***Confidentiality Protections for the Use of Genetic Services***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to protect the confidentiality of the fact that an individual has obtained and/or inquired about genetic testing and/or counseling. The statutes also should be amended to protect the confidentiality of the content of the inquiries and/or counseling.

***Scope of Consented-to Disclosure of Genetic Information by Persons Other Than the Subject of the Information***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to limit the disclosure of genetic information by persons other than the subject of the information to the amount necessary in light of the reason for the disclosure. The statutes also should be amended to limit such disclosures to those persons who have a need for the information in light of the reason for the disclosures.

***Permissible Third-Party Disclosures of Genetic Information without the Subject's Consent***

- Assuming that comprehensive medical confidentiality protections are not adopted, the legislature should review and, if appropriate, amend the genetic confidentiality statutes in light of the recommendations of the Special Committee on Medical Information Confidentiality of the New York State Public Health Council about legitimate disclosures of medical information without patient consent.

***Waivers of Genetic Confidentiality Protections***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York's genetic confidentiality statutes should be amended to render nonwaivable all of the confidentiality rights they provide.

***Disclosure of Genetic Information to Relatives***

- Health care providers should not disclose their patient's genetic information to the patient's relatives without the patient's consent or a court order. Courts should be authorized to permit health care providers to make such disclosures

only when (1) the patient refuses to disclose the information to an identified relative despite attempts by the health care provider to convince him or her to do so; (2) without disclosure, serious harm to the relative is highly likely to occur; (3) with disclosure, the harm can be averted or its chances of occurring significantly minimized; and (4) the harm that may result from failure to disclose outweighs the harm that may result from the disclosure.

***Court Orders for Disclosure of Genetic Information***

- Other than court orders for the disclosure of genetic information to a patient's relatives, New York law should be amended to permit court orders for the disclosure of genetic information to third parties without the subject's consent only when (1) absent the disclosure, there is or would be a clear and imminent danger to the public health; (2) the third party is entitled to the disclosure under federal and/or New York statutes or regulations; or (3) in a civil or criminal litigation, the subject of the information affirmatively places his or her physical or mental condition at issue and the genetic information to be disclosed directly relates to that physical or mental condition.

***Remedies for Unlawful Disclosure or Solicitation of Genetic Information***

- Assuming that comprehensive medical confidentiality protections are not adopted, New York law should be amended to (1) expressly authorize private lawsuits by victims of unlawful disclosures or solicitations of genetic information against persons who make such disclosures or solicitations and (2) authorize the Attorney General to bring lawsuits on behalf of individuals whose genetic information has been or will be unlawfully disclosed or solicited. In addition, persons and organizations licensed by New York State should be subject to professional discipline for unlawfully disclosing or soliciting genetic information.

***Anonymous Genetic Testing***

- New York law should be amended to eliminate potential barriers to anonymous genetic testing.

### Insurance

#### *Use of Genetic Test Results by Life, Disability, and Long-Term Care Insurers*

- New York insurance law should be amended to require a moratorium on requests for genetic test results and the use of genetic test results in underwriting, by life, disability, and long-term care insurers. Insurers should be permitted to use these results for underwriting only when (1) the subjects of the tests voluntarily provide the results to the insurer and (2) the insurers will use the results for the subjects' benefit.

### Public Health and Genetic Services

#### *Exemption from State Regulations for Laboratory Licensure*

- New York's Public Health Law, which requires state licensure for all laboratory tests performed on specimens obtained in New York, should be amended to permit the New York State Department of Health to grant exemptions on a case-by-case basis.

### Integrating Genetic Services into Clinical Care

#### *State Licensure or Certification of Genetic Counselors*

- New York State should create a process for state certification of genetic counselors who are certified by the American Board of Genetic Counseling or American Board of Medical Genetics.

## Regulatory Recommendations

### Newborn Screening

#### *Basic Requirements for Newborn Screening Tests*

- New York's Newborn Screening Program panel should be restricted to tests that detect congenital disorders characterized by serious and irreparable harm that can be avoided or minimized only by prompt application of confirmed medical interventions. The analytical and clinical validity of the screening tests also must be confirmed.

#### *Informing Parents about Newborn Screening*

- The Newborn Screening Program should provide educational materials about screening to prenatal care providers, as well as to hospitals and institutions of birth. Prenatal care providers should be required to provide and be available

to discuss these materials during the course of prenatal visits. Program materials should be multilingual and at appropriate reading levels for a general audience. They should explain the purpose of screening and provide a description of the disorders screened for, their population incidence, and the follow-up process for infants with a positive screen test result.

## *Establishment of a Newborn Screening Advisory Committee*

- New York's public health regulations should establish a newborn screening advisory committee to act in an advisory capacity to the Commissioner of Health and the Newborn Screening Program. The committee should include outside professional and community representatives and should be independent from the screening program. It should meet at least annually to consider new screening tests, solicit community input, and evaluate program infrastructure, policies, and outcomes.

### *Review and Implementation of Newborn Screening Tests*

- A newborn screening advisory committee, and ad hoc specialty subcommittees established by it, should review all tests currently on or under review for New York's screening panel, as well as potentially valuable new tests, and make recommendations to the Commissioner. For tests for which a confirmed medical benefit has not been sufficiently demonstrated, tests should be viewed as human subject research and should require parental informed consent. These tests should be subject to review by an institutional review board to determine the information that should be provided as part of obtaining parental informed consent. All new screening tests should be subject to periodic follow-up evaluation to determine test accuracy and effectiveness of medical interventions.

### *Research Use of Anonymized Newborn Bloodspots*

- The Newborn Screening Program, consistent with the recommendations in Chapter 7 concerning research use of samples obtained in the clinical context, should permit the use of anonymized samples for research. The program should inform parents that residual bloodspots may be anonymized and used for quality assurance activities or research. Parents should be informed of the potential research value of the samples and of the impossibility of linking research results to any individual newborn.

*Research Use of Identified Newborn Bloodspots*

- Research use of identified newborn bloodspots should be permitted in accord with recommendations in Chapter 7 concerning the research use of identified samples obtained in the clinical context. In addition, investigators who seek to use identified newborn blood samples for research should demonstrate why unidentified samples or alternate sample sources would not suffice. The use of identified samples should require recontact by the New York State Department of Health and informed consent of parents for each research use. The New York State Department of Health should not release samples that retain identifying data to researchers outside the department except for rare circumstances in which the research is directly relevant to the health of a specific newborn.

## *Research Use of Coded Newborn Bloodspots*

- Research use of coded newborn bloodspots should be permitted in accord with recommendations in Chapter 7 concerning the research use of coded samples obtained in the clinical context. The use of coded samples should require recontact by the New York State Department of Health to obtain the consent of parents for the future research use of the samples.

## *Policies for Storage of Newborn Bloodspots*

- The Newborn Screening Program should establish a formal policy for the storage of residual identified and anonymized bloodspots. The policy should specify potential uses for stored bloodspots and a maximum period of time for which samples may be maintained with personal identifiers.

### ***Notification of Parents of Newborn Carrier Status***

- New York's Newborn Screening Program should report a newborn's carrier status to the authorized physician.

### **Informed Consent**

### ***Content of Informed Consent to Genetic Testing in the Clinical Context***

- Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require the following information to be provided to the patient before obtaining the patient's consent (elements currently not required by New York law are italicized):

    1. The purpose of the test

2. A general description of the testing process

3. A description of the diseases or conditions tested for, *including their ranges of severity*

4. *The risks and benefits of, and alternatives to, the predictive genetic test*

5. Confidentiality issues, *including confidentiality protections, the circumstances under which results of tests may be disclosed without the patient's consent*, and the names of persons and/or organizations to whom the patient has consented to disclose the results

6. *Protections against adverse uses of genetic information*

7. *The chances of false positive and false negative results*

8. The meaning of both positive *and negative* results

9. *The ability, or lack thereof, of the test to predict a disease's severity and age of onset*

10. *The possibility that no additional risk information will be obtained at the completion of the test*

11. *Available medical surveillance, treatment, and/or reproductive options following testing*

12. A statement that, prior to providing informed consent to genetic testing and after receiving the results, the individual may wish to obtain professional genetic counseling

13. *The risks of transmitting the relevant mutation to children and that the mutation may be present in other blood relatives*

14. A statement that no tests other than those authorized will be performed on the biological sample and that the sample will be destroyed at the end of the testing process, or not more than a specific period of time after the sample was taken, unless the subject consents to a longer period of storage

15. *That the test is voluntary*

16. *An offer to answer inquiries*

17. *The fees charged for the laboratory tests and pre- and posttest counseling*

***Persons Required to Obtain Informed Consent***

- Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require that the person who orders a genetic test has the obligation to ensure that the subject's informed consent is obtained.

***Responsibility of Testing Laboratories***

- The New York State Department of Health should permit clinical laboratories to perform predictive genetic tests on biological samples only if the laboratories receive assurances that the subjects provided informed consent for the tests.

***Informed Consent to Multiplex Genetic Testing***

- Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, generic consent to multiplex testing should be permitted if (1) the number of tests on the panel is so high or the information about the tests is so complicated that attempting to obtain full informed consent from the patient to each test would be confusing or otherwise burdensome to the patient; (2) the tests on the panel meet all of the criteria described in Chapter 5 for inclusion in a multiplex panel; (3) the patients are informed, prior to testing, that more detailed information about each test is available; and (4) the patients are given an opportunity to obtain that information prior to testing either from the health care provider offering the multiplex panel or from another health care professional.

***Sufficiency of Signed Informed Consent Form as Evidence of Informed Consent***

- Assuming that New York law is amended to authorize the Commissioner of Health to regulate informed consent to predictive genetic testing, the Commissioner should require that health care providers disclose informed consent information in a manner that will enable the patient to make a knowledgeable evaluation. A signed informed consent form is not necessarily sufficient evidence that this goal has been achieved.

**Public Health and Genetic Services**

***Approval for Genetic Tests***

- Laboratories with New York State permits to perform genetic tests should provide appropriate educational materials to providers ordering the test.

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